

#### Amsterdam Molecular Therapeutics (AMT) Holding N.V.

(a public limited liability company incorporated under the laws of the Netherlands with its corporate seat in Amsterdam)

#### Admission to listing and trading of up to €16.3 million in new ordinary shares

This prospectus (the "**Prospectus**") is published in relation to the admission to listing and trading of up to €16.3 million in new ordinary shares in the capital of Amsterdam Molecular Therapeutics (AMT) Holding N.V. with a nominal value of €0.04 per ordinary share (the "**New Shares**"). The New Shares shall be issued pursuant to an offering outside of the United States in "offshore transactions" within the meaning of, and pursuant to, Regulation S under the U.S. Securities Act of 1933, as amended (the "**Securities Act**") by means of a private placement to certain institutional investors, other qualifying investors who subscribe for at least €50,000 per investor in various jurisdictions and the members of the Board of Management (the "**Private Placement**") (see also "Private Placement").

Capitalized terms used but not otherwise defined in this Prospectus are defined in "Definitions and Glossary". In this Prospectus, "Company" refers to Amsterdam Molecular Therapeutics (AMT) Holding N.V. and "we", "our", "us" and similar terms refer to Amsterdam Molecular Therapeutics (AMT) Holding N.V. and its subsidiaries unless explicitly stated to the contrary. Any reference to "shares" and "our shares" shall refer to the Company's shares, including the New Shares, outstanding from time to time.

There is a high degree of risk relating to our business, our company and any investments in our shares. These risks are described under "Risk Factors" beginning on page 10 of this Prospectus and should be timely and carefully considered by any investor.

The shares currently outstanding are listed and traded on NYSE Euronext in Amsterdam ("**Euronext Amsterdam**") under the symbol "AMT" and ISIN Code NL0000886968. On 4 October 2010, the closing price of our shares on Euronext Amsterdam was €2.00 per share.

The Private Placement shall be structured as an accelerated bookbuilt offering starting on 5 October 2010 immediately after the publication of this Prospectus and expected to close on 7 October 2010, subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances. The issue price for the New Shares to be issued pursuant to the Private Placement (the "Issue Price") will be determined on the basis of the accelerated bookbuilding process. Together with the actual number of New Shares issued pursuant to the Private Placement and the proceeds of the Private Placement, the Issue Price shall be incorporated in a pricing statement which will be deposited with the Netherlands Authority for the Financial Markets (Stichting Autoriteit Financiële Markten, "AFM") and published in a press release and on our website on or about 7 October 2010, subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances. The Private Placement is subject to certain customary conditions. We are not taking any action to permit a public offering of the New Shares in any jurisdiction. The statutory pre-emptive rights (voorkeursrechten) of the holders of our shares shall be excluded with respect to the Private Placement. For more information on the Private Placement, see "Private Placement" in this Prospectus.

We will apply for admission of the New Shares to listing and trading on Euronext Amsterdam. We expect that trading in the New Shares on Euronext Amsterdam will commence on or about 12 October 2010, subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances.

Subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances, payment and settlement of the New Shares which shall be issued pursuant to the Private Placement is expected to occur on or about 12 October 2010. Delivery of the New Shares shall take place through the book-entry facilities of Nederlands Centraal Instituut voor Giraal Effectenverkeer B.V. ("Euroclear Netherlands") only, in accordance with its normal settlement procedures applicable to equity securities and against payment for the New Shares in immediately available funds.

The New Shares shall be offered and sold outside the United States, in "offshore transactions" within the meaning of, and pursuant to, Regulation S under the Securities Act, to investors that are not US Persons (as such term is

defined in Regulation S under the Securities Act). The New Shares have not been approved or disapproved by the United States Securities and Exchange Commission or any securities commission or other regulatory authority of any state or other jurisdiction of the United States, 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. The New Shares have not and will not be registered under the Securities Act or under any securities laws of any state or other jurisdiction of the United States and may not be taken up, offered, sold, resold, delivered or distributed, directly or indirectly, in or into or from the United States except pursuant to an applicable exemption from, or in a transaction not subject to, the registration requirements of the Securities Act and in compliance with the securities laws of any state or other jurisdiction of the United States. There will be no public offer in the United States nor in any other jurisdictions.

This Prospectus does not constitute an offer to sell, or solicitation of an offer to buy, any of the New Shares or any other securities issued by us. The distribution of this Prospectus may be restricted by law in certain jurisdictions and therefore persons into whose possession this Prospectus comes should inform themselves of and observe any restrictions. For a description of restrictions on offers, sales and transfers of our shares and the distribution of this Prospectus, see "Selling and Transfer Restrictions".

This Prospectus may only be used in connection with the admission to listing and trading of the New Shares on Euronext Amsterdam. This Prospectus constitutes a prospectus for the purposes of article 5(3) of the Directive 2003/71/EC (the "**Prospectus Directive**") and has been prepared pursuant to article 5:2 of the Dutch Financial Supervision Act (*Wet op het financieel toezicht*) (the "**Financial Supervision Act**") and the rules promulgated there under. This Prospectus has been approved by and filed with the AFM on 5 October 2010.

The date of this Prospectus is 5 October 2010.

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### Summary

This summary provides an overview of selected information contained in this Prospectus and should be read as an introduction to this Prospectus. Any decision to invest in our shares, including the New Shares, should be based on consideration of the Prospectus as a whole. Any prospective investor should carefully read the Prospectus in its entirety before investing in our shares, including the information discussed under "Risk Factors" beginning on page 10 of the Prospectus, as well as our consolidated financial statements and the notes thereto that are incorporated by reference in the 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 the Prospectus. Where a claim relating to information contained in the 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 the Prospectus before the legal proceedings are initiated.

#### Summary of our business

#### Overview

We are a leader in the development of human gene based therapies. In December 2009, we filed a marketing authorization approval (MAA) with the European Medicines Agency (EMA) for Glybera®, our lead product, for Lipoprotein Lipase Deficiency (LPLD). We expect to be able to obtain an opinion from the EMA's Committee for Medicinal Products for Human Use (CHMP) on our filing in mid 2011. If this opinion is positive, a decision from the European Commission for marketing authorization is expected to follow approximately two months thereafter. This puts us in a leading position in the field of gene therapy companies competing to bring a gene therapy product to commercialization. Our goal is to leverage our leadership position in this highly innovative field of gene therapy to build a specialty biopharmaceutical company for rare, mostly orphan diseases.

Our pipeline consist of five programs. In addition to Glybera®, we have programs for Duchenne Muscular Dystrophy (AMT-080), Hemophilia B (AMT-060), Acute Intermittent Porphyria (AMT-021) and Parkinson's Disease (AMT-090).

Our lead product Glybera® is developed for the indication Lipoprotein Lipase Deficiency, a debilitating metabolic disorder. It has already demonstrated excellent results with clinically impressive effects in reducing the risk of pancreatitis while being well tolerated and generally safe. Pancreatitis is the most frequent, very painful and potentially life threatening clinical feature of LPLD. First sales of Glybera® for LPLD under a "named-patient-sales" program in France, are expected early 2011.

All of the programs in our pipeline are based on our Adeno Associated Virus (AAV)-based gene delivery technology platform and our baculovirus and insect cell based manufacturing platform. In focusing on AAV vectors, we are using gene delivery vehicles which are generally considered safe. We use different AAV vectors to target various organs or specific tissues, such as muscle or liver, and even to specific types of cells within these organs. By genetically engineering our AAV-based vectors with different therapeutic genes and tissue specific promoters we have a platform vector technology that is modular in approach, facilitating fast product design within short timelines.

We focus on developing innovative treatments for diseases with a significant unmet medical need. Our programs are either targeted at orphan diseases, or are driven by their potential to replace existing products that provide a sub-optimal level of care in substantial markets. For example, we aim to develop therapies which have the potential to improve existing, inferior treatments, and also to substitute an entire market through providing a real cure as opposed to offering only symptomatic treatment.

Whilst there are more than 45 AAV-based gene therapy trials ongoing, there are only a few which are in Phase III clinical trials or in registration. One of our core strengths is that our staff has extensive experience of developing and registering specialty drugs.

We are located in Amsterdam, the Netherlands. We currently have 84 employees and have a staff of highly educated, skilled and experienced professionals. In addition, we have a world-class,  $375\text{m}^2$ , cGMP-licensed manufacturing facility. In this highly specialized facility we have manufactured batches for the clinical trials and here we can also produce the material for all the clinical trials for the products we are currently developing. The facility is fully validated for commercial production and has a capacity capable of producing enough material to supply our European and North American target markets with Glybera® for LPLD and for the next phases of development of the other programs currently in our pipeline.

#### Summary of our strategy

Our mission is to serve patients with serious chronic progressive, often inherited disorders, by providing a cure with a single treatment intervention. The goal is to become a specialty biopharmaceutical company which develops gene therapy products for diseases with a significant unmet medical need, and market these ourselves or via partnerships.

Our strategy to achieve this goal is based on three main elements:

Validate the gene therapy approach through the approval of Glybera®

Glybera® for LPLD is currently first in line for marketing authorization in Europe among all gene therapy products. If approved, this drug not only validates our capabilities and know how in bringing novel therapeutic cures to market, but also validates gene therapy in general as an innovative treatment approach.

• Focus on innovative treatments for diseases with significant unmet medical need

We focus on building a specialty biopharmaceutical company delivering innovative treatments for diseases with a significant unmet medical need. Our programs are either targeted at orphan diseases, or are driven by their potential to replace existing products that provide sub-optimal solutions for substantial markets.

#### • "Build and partner" approach

We intend to be a company that develops products that we can commercialize ourselves as well as products which are more suited for commercialization via partnerships. We will aim to conclude such partnerships relatively early to generate revenues to provide non-dilutive funding. In general, we intend to commercialize products targeted at orphan diseases ourselves, whilst we believe that programs aimed to replace existing products could have much potential for lucrative early stage partnering.

Transaction opportunities, such as mergers and acquisitions, partnerships or collaborations, licensing transactions and acquisitions of additional pipeline products, technology or intellectual property, which may accelerate the path to sustainable and profitable growth or otherwise be beneficial to our business will always be considered in the normal course of our business.

#### Key technologies and capabilities

We have developed a broad platform that we believe has helped to overcome major challenges which the gene therapy industry was facing. The following key technologies and capacities clearly differentiate our approach from other gene delivery systems:

- Our platform vector technology
- Our platform manufacturing technology
- Our clinical development and regulatory expertise
- Our modular platform focused approach

#### Key financial data

(6:- 11		nded 30 June			
(€ in thousands)	2010	2009	2009	2008	2007
	una	udited			
Total net income	563	85	355	223	110
Research and	(8,128)	(7,070)	(13,241)	(13,118)	(9,804)
development costs					
General and	(1,765)	(2,914)	(4,913)	(5,895)	(4,966)
administrative costs		,			
Total operating	(9,893)	(9,984)	(18,154)	(19,013)	(14,770)
costs		,			
Operating result	(9,330)	(9,899)	(17.799)	(18,790)	(14,660)
Result for the	(9,351)	(9,423)	(17,175)	(16,919)	(14,935)
period		,			
Earnings per share	(0.63)	(0.64)	(1.17)	(1.16)	(1.28)
Cash and cash	13,511	25,863	22,624	34,150	51,330
equivalents					
Equity	9,108	25,682	18,410	35,105	51,407

#### Principal risks

The following factors represent the principal risks associated to our business, our company and our shares, including the New Shares. These risks are more fully described under "Risk Factors" beginning on page 10.

Risks related to our business and our company

 A substantial part of our future commercial potential depends on our lead product Glybera®

- We are dependent on additional funding, which may not be available to us on acceptable terms, or at all, which could force us to delay or impair our ability to develop or commercialize our products.
- Any failure or delay in commencing or completing clinical trials for our products could severely harm our business.
- The regulatory approval process is costly and lengthy and we may not be able to successfully obtain all required regulatory approvals.
- Even if our products receive marketing approval they will remain subject to ongoing regulatory review. If we fail to comply with continuing regulations, we could lose these approvals.
- Our success is dependent on our ability to obtain or maintain orphan drug designation and/or orphan drug status and to be first to market in order to ensure subsequent marketing exclusivity for a large part of our product pipeline.
- Our future success will depend upon our ability to enter into partnerships with third parties.
- We may not be able to protect our technology and enforce our intellectual property rights adequately.
- We rely on intellectual property rights, many of which are in-licensed from third parties.
- In order to further develop our products we may need to obtain rights to additional intellectual property.
- Litigation or third party claims alleging intellectual property infringement could require substantial time, manpower and money to resolve. Unfavorable outcomes in these proceedings could limit our intellectual property rights and/or our activities.
- Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.
- We may be unable to compete effectively against new technologies or competitors that have developed or develop products that are cheaper, more effective or safer than ours.
- We face rapid technological change.
- If we do not comply with laws regulating the protection of the environment and health and safety or cGMP standards, our business could be adversely affected.
- Our products may not gain market acceptance.
- Adverse events in the field of gene therapy could damage public perception of our products and negatively affect governmental approval and regulation.
- Our ability to generate revenue from any products that we may develop will depend on reimbursement and pricing policies and regulations.

- Our ability to generate revenue may be dependent on new pricing strategies and a new business model.
- We may become exposed to costly and damaging product liability claims and may not be able to maintain sufficient product liability insurance to cover these claims.
- Interrupted product supply or development as a result of an unforeseen event may delay and/or damage our ability to generate revenues and our likelihood of success will be harmed.
- Our products are based on a single underlying technology based on gene therapy using adeno-associated viral vectors.
- Our success depends substantially on our most advanced products, which are either still in the registration process or in clinical and pre-clinical development. If we are unable to bring these products to market, or experience significant delays in doing so, our ability to generate product revenue and our likelihood of success will be harmed.
- Only one product using baculovirus production technology has as yet been approved.
- We have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future. We may never become profitable.
- We rely on third parties for pre-clinical development activities, clinical trials and to support our regulatory submissions. If these third parties do not perform as contractually required or expected, we may not be able to develop, obtain regulatory approval for or commercialize our products.
- We rely on the skills and expertise of our key personnel and secondees, and our future depends on our ability to attract and retain qualified personnel.
- We rely on collaborative relationships to further develop our business and if we or any
  of our current or future collaborators fail to perform or terminate any obligations under
  our collaborative arrangements, our programs could be delayed or terminated.
- We may fail to select or capitalize on the most scientifically, clinically or commercially promising or profitable products.
- We may encounter difficulties in managing future growth.
- Our information technology systems could face serious disruptions that could adversely affect our business.
- Exchange rate fluctuations could negatively affect our financial condition.

#### Risks related to our shares, including the New Shares

- The ownership of our shares is highly concentrated with a small number of shareholders who may be in a position to exert significant influence over our management and operations and whose interests may conflict with those of other shareholders
- The price of our shares may be volatile and affected by a number of factors, some of which are beyond our control.

- The volume of trading in our shares has historically been low.
- The price and trading volume of our shares could decline depending on market appraisal.
- We do not intend to pay dividends for the foreseeable future.
- 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.

#### Corporate information

Amsterdam Molecular Therapeutics (AMT) Holding N.V. is a public limited liability company (naamloze vennootschap) incorporated under the laws of the Netherlands with its corporate seat and registered office in Amsterdam Zuidoost, the Netherlands and registered with the Commercial Register in the Netherlands under number 33301321. Our business address is Meibergdreef 61, 1105 BA Amsterdam Zuidoost, the Netherlands. We currently conduct our business from the Netherlands and have 84 employees.

#### **Risk Factors**

There is a high degree of risk relating to our business, our company and any investments in our shares. If any of the following risks and uncertainties actually occur, our business, financial condition and/or results of operations could be materially and adversely affected. In such a case the market price of our shares could decline and investors may lose all or part of their investment.

The risks and uncertainties described below are a list of risks and uncertainties in relation to our business, our company and our shares currently known to us and which we deem material. Additional risks and uncertainties, not presently known to us, or which we currently deem immaterial, may also have a material adverse effect on our business, financial condition, results of operations and/or prospects and could negatively affect the price of our shares. All these factors are contingencies which may or may not occur. We may face one or more of the risks and uncertainties described below simultaneously.

The order in which the following risks are presented is not intended to be an indication of their probability of occurrence or the magnitude of their potential effects.

#### Risks related to our business and our company

### A substantial part of our future commercial potential depends on our lead product Glybera®

Our main short term goal is to commercialize Glybera® - our lead product for Lipoprotein Lipase Deficiency (LPLD). In December 2009, we filed Glybera® for LPLD for marketing authorization with the European Medicines Agency (EMA). We expect to be able to obtain an opinion from the EMA's Committee for Medicinal Products for Human Use (CHMP) on our filing in mid 2011. If this opinion is positive, a decision from the European Commission for marketing authorization is expected to follow approximately two months thereafter. We expect to be able to file for market approval in Canada with Health Canada in 2011 and in the United States with the Food and Drug Administration (FDA) by the end of 2011 or early in 2012.

If we fail to obtain marketing authorization for Glybera® for LPLD in the European Union, Canada and/or the United States, then our business, financial condition, results of operations and prospects will be adversely affected. Our business may also be harmed if the regulatory process is delayed or requires us to treat additional patients or generate or collect additional data. We expect that if we are granted marketing authorization in the European Union, the authorization granted to us shall be a "marketing authorization based on exceptional circumstances", which will require us to implement risk management procedures, subject us to certain notification obligations and will result in the authorization being subject to annual re-assessment (see "Government regulation and product approval — General regulation in the European Union — Marketing approval"). Failure to obtain marketing authorization for Glybera® for LPLD may also adversely affect our ability to develop other programs in our pipeline, given the general applicability of our technology platform to the development of the programs we currently have in our pipeline and may develop in the future.

If marketing authorization for Glybera® for LPLD is obtained, our business, financial condition, results of operations and prospects may be adversely affected if we are unable to successfully commercialize Glybera® for LPLD - ourselves or via partnerships - or in case the market for or revenues from sales of Glybera® for LPLD are disappointing. Factors which

may influence the successful commercialization of Glybera® for LPLD include the extent to which patients can be identified and diagnosed, the extent to which reimbursement for Glybera® for LPLD will be available and the amount that we will be able to charge for the product.

We are dependant on additional funding, which may not be available to us on acceptable terms, or at all, which could force us to delay or impair our ability to develop or commercialize our products.

As at 30 June 2010 our cash resources amounted to €13.5 million and as at 31 August 2010 to €11.3 million. Since then, in line with budget and in the ordinary course of business our cash resources have further decreased and are expected to be depleted in the second quarter of 2011 if no additional cash is received. Accordingly, our current cash resources do not provide us with sufficient working capital for the next twelve months following the date of this Prospectus and additional funds are therefore required (see also "Operating and Financial Review – Working capital statement" and "Operating and Financial Review – Outlook"). If we succeed at raising additional funds to provide us with sufficient working capital for the next twelve months following the date of this Prospectus, we expect that in the future we may again need additional funding, as we have not yet reached the point of generating profits that could fund our operations nor can we be certain that we will reach that point in the near term.

There can be no assurance that additional funds will be available on a timely basis, on favorable terms, or at all, or that such funds, if raised, would be sufficient to enable us to continue to implement our long term business strategy. If we are unable to raise such additional funds through equity or debt financing, we may need to delay, scale back or cease expenditures for some of our longer term research, development and commercialization programs, or grant rights to develop and market products that we would otherwise prefer to develop and market ourselves, thereby reducing their ultimate value to us. It may also result in us not being able to continue as a going concern, which could have a material impact on the carrying value of, in particular, intangible assets and property, plants and equipment. Our inability to obtain additional funds necessary to operate the business could furthermore materially and adversely affect the market price of our shares and all or part of an investment in our shares could be lost. In addition, to the extent we raise capital by issuing additional shares, shareholders' equity interests would be diluted.

The amount and timing of any expenditure required to implement our business strategy and continue the development of our products will depend on many factors, some of which are out of our control, including but not limited to:

- scope, rate of progress, results and cost of our pre-clinical and clinical trials and other research and development activities;
- terms and timing of any collaborative, licensing and other arrangements that we may establish;
- higher cost, slower progress than expected to develop products and delays in obtaining regulatory approvals;
- number and characteristics of products that we pursue;
- cost and timing of establishing sales, marketing and distribution capabilities;

- timing, receipt and amount of sales or royalties, if any, from our potential products, or any up-front or milestone payments during their development phase;
- the cost of preparing, filing, prosecuting, defending and enforcing any intellectual property rights; and
- the extent to which we acquire or invest in businesses, products or technologies.

### Any failure or delay in commencing or completing clinical trials for our products could severely harm our business.

To obtain the requisite regulatory approvals to market and sell any of our products, we must demonstrate through extensive pre-clinical and clinical trials that the products are safe and efficacious in humans. Pre-clinical and clinical trials are expensive, can take many years and have an uncertain outcome. A failure of one or more of our pre-clinical or 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 later stage clinical trials or product approval by the EMA, the FDA, Health Canada or any other regulatory authority. Products that show positive pre-clinical or early clinical results often fail in later stage clinical trials. We may not be able to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of patients, retain enrolled patients, or begin or successfully complete clinical trials in a timely fashion, if at all. Any failure to perform may delay or terminate the trials.

To date, we have carried out clinical trials only in respect of Glybera® - our lead product for Lipoprotein Lipase Deficiency (LPLD) – for which we submitted the marketing authorization application with the EMA in December 2009. We have not commenced any clinical trials required for the approval of any other program in our pipeline. The commencement and completion of clinical trials for any or all of our programs may be delayed, suspended or terminated as a result of many factors, including but not limited to:

- the delay or refusal of regulators or institutional review boards, independent ethics committees or ethical review boards to authorize us to commence a clinical trial at a prospective trial site:
- delays in patient enrolment and variability in the number and types of patients available for clinical trials, which may result in additional costs and delays;
- lower than anticipated retention rates of patients and volunteers in clinical trials and/or difficulty in maintaining contact with patients after treatment, resulting in incomplete data, including data on efficiency and duration of cure;
- negative or inconclusive results, which may require us to conduct additional pre-clinical or clinical trials or to abandon projects that we expect to be promising;
- poor effectiveness/efficacy of products during clinical trials;
- unforeseen safety issues or side effects;
- exceeding budgeted costs due to difficulty in predicting accurately costs associated with clinical trials;

- unfavorable governmental or regulatory inspection and review of our premises, 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 pre-clinical or clinical trials for any of our products, or requirement by a regulatory authority to carry out additional pre-clinical or clinical trials, would delay commercialization of our products and severely harm our business and financial condition. It is also possible that, for any of our products, we will not complete clinical trials in any of the markets in which we intend to sell those products. Accordingly, we would not receive the regulatory approvals needed to market our products.

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

Pre-clinical development, clinical trials, manufacturing, marketing and labeling of pharmaceuticals and medical devices are all subject to extensive regulation by governmental authorities and agencies in the EU, the US and other jurisdictions. We must obtain regulatory approval for products 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 EMA, the FDA or any other applicable regulatory agency will take or whether any such approvals ultimately will be granted. The EMA, 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 regulatory approval process include delays or rejections based on the failure of clinical or other data to meet expectations, or the failure of the entire product or medical device to meet a regulatory agency's requirements for safety and efficacy.

Additional clinical trials may be required if clinical trial results are negative or inconclusive, or in the event that a regulatory agency requires additional clinical data to be generated, which will require us to incur additional costs and significant delays. If we do not receive the necessary regulatory approvals, we will not be able to generate product revenues and may not become profitable. We may encounter significant delays in the regulatory process. This could result in excessive costs that may prevent us from continuing to develop our products.

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.

# Even if our products receive marketing approval they will remain subject to ongoing regulatory review. If we fail to comply with continuing regulations, we could lose these approvals.

Even if we receive regulatory approval to market a particular product, the approval could be conditional on us conducting additional costly post-approval studies or could limit the indicated uses included in the labeling of our products. Moreover, the product may later cause adverse effects that limit or prevent its widespread use, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. In addition, as the manufacturer of the product, we, and our 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 the product will remain subject to extensive regulatory requirements.

If we fail to comply with applicable regulatory requirements or previously unknown problems with our products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including but not limited to:

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

Our success is dependent on our ability to obtain or maintain orphan drug designation and/or orphan drug status and to be first to market in order to ensure subsequent marketing exclusivity for a large part of our product pipeline.

An important element of our strategy is to develop products in indications qualifying for orphan drug status in order to obtain marketing exclusivity. If a product is designated as an orphan drug, such product may gain orphan drug status upon regulatory approval to market and sell such product. Orphan drug status confers the right to exclusively market the product for the specified disease for seven years in the US and for ten years in the EU. To date, we have been granted orphan drug designation for our lead product Glybera® for LPLD and for our AMT-080 product for Duchenne Muscular Dystrophy in the US and the EU as well as our AMT-021 product for Acute Intermittent Porphyria in the EU. There is no guarantee that we will be able to obtain and maintain orphan drug status and marketing exclusivity for all or any of our products in the EU or the US. Orphan drug designation may be obtained for the same product in the same indication by several parties and only the first party to obtain marketing authorization receives orphan drug status and marketing exclusivity. If a third party were to obtain orphan drug status and marketing exclusivity for the product and in the indication targeted by us, we may be excluded from marketing that product. Also, once granted, marketing exclusivity may be revoked or exceptions to marketing exclusivity may be granted to other third parties, for example if we are unable to supply sufficient quantities of the product, if a potential product based on the same technology of a third party is clinically superior, or as a consequence of regulatory changes or for other reasons. The results of our operations and financial and commercial prospects could be materially adversely affected if our lead product were to lose orphan drug designation in the US or the EU, if we fail to obtain and maintain orphan drug designation and/or status for our other indications or products, or if

the commercial value of such designation and/or status is generally diminished in any material respect.

## Our future success will depend upon our ability to enter into partnerships with third parties.

Our strategy for the commercialization of some of our products, in particular those for larger indications, is to partner or out-license such products to third parties. If we are not able to locate, and enter into favorable agreements with, suitable third parties we will have difficulty commercializing the relevant products.

The process of establishing partnerships is difficult, time-consuming and involves significant uncertainty. Moreover, even if we establish such relationships, it may be difficult to maintain or perform under such arrangements, as funding resources may be limited or our partners 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 partners 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 partnership 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 partners.

Our ability to predict the success of any partnership we may enter into is limited due to (amongst others) the complexity and uncertainty of these arrangements. Partnership agreements typically involve a complex allocation of responsibilities, costs and benefits. Such 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 partnerships.

# We may not be able to protect our technology and enforce our intellectual property rights adequately.

Our ability to compete effectively with other companies depends, amongst other things, on protection of our technology and enforcement of our intellectual property rights and the intellectual property rights we have in-licensed.

No assurance can be given that we will develop products which are patentable or that any pending or future patent application seeking patent or other protection for our technologies that is material to one or more of our products will be granted. The lack of any such patents may have a material adverse effect on our ability to develop and market our proposed products. There can be no assurance as to the ownership of any patents in which we have an interest or that claims relating to such patents will not be asserted by other parties. Our attempts to obtain or maintain patent or other protection for our technologies may also be subject to opposition, interference, revocation or other proceedings, which may require us to incur substantial costs to overcome, with no guarantee of success. Even if, and to the extent that, patent protection is obtained and maintained, no assurance can be given that patents, or the patents we have in-licensed, will be sufficiently broad in scope to provide commercially meaningful protection against competition from third parties or that we will successfully commercialize our products or technologies prior to expiry of the patent protection.

### We rely on intellectual property rights, many of which are in-licensed from third parties.

We rely on intellectual property rights to protect our technology. Many of the intellectual property rights we use and on which we propose to rely have been licensed to us by third parties. There can be no assurance that any intellectual property rights licensed to us by third parties will be free from the rights and interests of further third parties or that the licensor had or will have the right or ability to confer on us any right, title or interest in any such intellectual property right. Further, there can be no assurance that such intellectual property right is valid and enforceable. Where intellectual property rights are licensed to us there can be no guarantee that the licensor will adequately maintain and protect the underlying intellectual property rights in which we have an interest. Should some or all of the patents that we rely on expire, be or become invalid or unenforceable, or if some or all of our or our licensors' patent applications not give rise to issued patents or give rise to patents with only narrow claims, we may be subject to competition from third parties with similar products. In particular, a failure by a licensor to maintain or enforce the patent protection in which we have an interest could prejudice our ability to develop products and our ability to prevent competitors utilizing our product technologies. This could severely harm our business and financial condition and the results of our operations.

Where intellectual property rights are licensed to us there can be no assurance that our rights to such intellectual property will not be suspended, terminated or otherwise lost in consequence of the breach of any agreement by us or due to other relevant facts or circumstances, for example, the insolvency of the licensor. Additionally, rights licensed to us may be limited in duration, application, field of use or territory or contain covenants restricting our freedom to conduct our business. Such limitations and restrictions may prove to be detrimental to the development of one or more of our products. Furthermore, laws, rules and regulations in certain jurisdictions may not recognize an agreement conferring an interest in intellectual property rights on us, or may hold that such agreement is invalid or void in whole or in part. We may be unable to register with relevant government agencies our in-licensed rights and licenses and may, as a result, be unable to enforce those rights to the technology independently of the licensor. An agreement conferring intellectual property rights to us, or by which we confer such rights on a third party, may be held in breach of competition laws in certain jurisdictions.

A breach of competition law may result in us being held liable to pay damages to third parties and/or a fine or other sanction and the unenforceability, termination or amendment of any agreement to which we may be a party.

# In order to further develop our products we may need to obtain rights to additional intellectual property.

The technical field in which we operate is highly complex involving many different intellectual property rights, including patents rights, know how and proprietary materials. At any stage of a product's lifecycle there may be additional intellectual property identified or developed that we may require rights to in order to further develop our products.

We may not be able to develop or commercialize products because of patent protection others have or will have. Our business will be harmed if we cannot obtain a necessary or desirable license, can obtain such a license only on terms we consider to be unattractive or unacceptable, or if we are unable to redesign our products or processes to avoid actual or potential patent or other intellectual property infringement. In addition, the granting of patent protection or orphan drug status or designation in respect of any of our products does not guarantee us freedom to operate and is separate to the risk of possible infringement by us of patents owned by third parties.

We cannot guarantee that there will be no claims from third parties alleging that our products infringe their intellectual property rights. Third parties may assert that we are employing their proprietary technologies without authorization and they may resort to litigation to attempt to enforce their rights. Third parties may have or obtain patents and claim that the use of our technology or any of our products infringes their patents. There could be no guarantee that we would be able to successfully defend ourselves against any such claim. Infringement or alleged infringement of patents may force us to take additional licenses to third party patents which will result in additional expenditure for us and may also cause delay in the development or commercialization of our programs or products.

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

We may need to resort to litigation to enforce or defend our intellectual property rights, including any patents issued to us. If a competitor or collaborator files a patent application claiming technology also invented by us, in order to protect our rights, we may have to participate in an expensive and time-consuming entitlement or opposition or revocation proceedings before the European Patent Office, the United States Patent and Trademark Office or patent authorities in other jurisdictions.

Our efforts to obtain, protect and defend our patent and other intellectual property rights, whether we are successful or not, can be expensive and may require us to incur substantial costs, including the diversion of management and technical personnel. An unfavourable ruling in patent or intellectual property litigation could subject us to significant liabilities to third parties, require us to cease developing, manufacturing or selling the affected products or using the affected processes, require us to license the disputed rights from third parties, or result in awards of substantial damages against us. During the course of any patent litigation, there may be public announcements of the results of hearings, motions and other interim proceedings or developments in the litigation. If securities analysts or investors regard these announcements as negative, the market price of the shares may decline. General proclamations or statements by key public figures may also have a negative impact on the perceived value of our intellectual property.

There can be no assurance that we would prevail in any intellectual property infringement action or will be able to obtain a license to any third party intellectual property rights on commercially reasonable terms, successfully develop non-infringing alternatives on a timely basis, or license non-infringing alternatives, if any exist, on commercially reasonable terms.

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

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

We may be unable to compete effectively against new technologies or competitors that have developed or develop products that are cheaper, more effective or safer than ours.

The pharmaceutical and biotechnology industries are highly competitive. Any products that we successfully develop may compete with existing and future therapies. There are many organizations, including pharmaceutical companies, biotechnology companies, academic laboratories, research institutions, governmental agencies and public and private universities, which are actively engaged in developing products that target the same markets as our products. Many of these competitors have substantially greater financial, technological, manufacturing, marketing, managerial and research and development resources and experience than we do. Many of these organizations also have much more experience than we do in pre-clinical and clinical trials of new drugs and in obtaining regulatory approvals. Accordingly, our competitors may succeed in developing competing technologies and products more rapidly than we do.

Our products, if successfully developed and approved for commercial sale, will compete with a number of drugs and therapies currently manufactured and marketed by major pharmaceutical and biotechnology companies. Our products 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 efficacious but cheaper, than our products. If our competitors develop and market products that are safer, more efficacious or cheaper, or develop, obtain regulatory approval and market such products earlier than we do, our commercial opportunity will be reduced or eliminated.

#### We face rapid technological change.

Our success depends, in part, on maintaining a competitive position in the development of products and technologies in a rapidly evolving field. Within the pharmaceutical and biotechnology industries, major technological changes can happen quickly. Rapid technological change, or the development by competitors of technologically improved or different drug delivery systems or products, could render our platform technologies or products obsolete or non-competitive. In the event that a new standard of care emerges for one of our products, it may result in our product becoming obsolete.

### If we do not comply with laws regulating the protection of the environment and health and safety or cGMP standards, our business could be adversely affected.

Our research and development involves the controlled use of limited amounts of biological materials and chemicals which require special handling and disposal. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by governmental and industry regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, the handling of biohazardous materials and cGMP standards. Additional European and local laws and regulations affecting our operations may be adopted in the future and if our operations were to expand into the United States, for example, we will be subject to additional legislation and regulation. We may incur substantial costs to comply with, and substantial fines or penalties (e.g. the revocation of a permit) if we violate, any of these laws or regulations.

#### Our products may not gain market acceptance.

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 efficacious from a therapeutic and cost perspective relative to competing treatments. We cannot predict whether physicians will make this determination in respect of our products.

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

- 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 payers;
- lack of cost-effectiveness;
- timing of market introduction of competitive products; and
- lack of reimbursement.

Even if our products achieve market acceptance, the market may prove not to be large enough to allow us to generate significant revenues.

## Adverse events in the field of gene therapy could damage public perception of our products and negatively affect governmental approval and regulation.

Public perception of our products could be harmed by negative events in the field of gene therapy. Serious adverse events, including patient deaths, have occurred in gene therapy clinical trials. Adverse events in our clinical trials and the resulting publicity, as well as any other adverse events in the field of gene therapy that may occur in the future, could result in a decrease in demand for any products that we may develop. The commercial success of our products will depend in part on public acceptance of the use of gene therapy for the treatment of human diseases. If public perception is influenced by claims that gene therapy is unsafe, our products may not be accepted by the general public or the medical community.

Future adverse events in gene therapy or the biotechnology industry could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our products. Any increased scrutiny could delay or increase the costs of our product development efforts and delay regulatory approval of our products.

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

Our ability to commercialize our products may depend, in part, on the extent to which reimbursement for our products will be available from government and health administration authorities, private health insurers, managed care programs and other third-party payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. In many countries, healthcare and pharmaceutical products are subject to a regime of reimbursement by government health authorities, private health insurers or other organizations. There is increasing pressure from these organizations to limit healthcare costs by restricting the availability and level of reimbursement. While we anticipate pricing our products consistent with current innovative, and new, mainly orphan medicines, there can be no assurance that adequate public health services or health insurance coverage will be available to enable us to obtain or maintain prices for our products sufficient to realize an appropriate return on investment.

In addition, changes to the rules and regulations regarding reimbursement or changes to existing regimes or reimbursement or the introduction of a new regime in any country could impact on whether reimbursement is available at adequate levels or at all. Rules and regulations regarding reimbursement may change frequently, in some cases at short notice. In Europe, the US and other territories there have been, and we expect that there will continue to be, a number of legislative and regulatory proposals aimed at changing the healthcare system. In view of the global cost pressures on healthcare and pharmaceutical markets, further changes should be expected.

In addition, third-party payers increasingly are challenging prices charged for pharmaceutical products, and many third-party payers may refuse to provide reimbursement for particular drugs when an equivalent generic or non-generic drug is available. Even if we show improved efficacy or improved convenience of administration with our product, pricing of the existing drug may limit the amount we will be able to charge for our product. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products, and may not be able to obtain a satisfactory financial return on products that we may develop.

### Our ability to generate revenue may be dependent on new pricing strategies and a new business model.

Our therapies are intended as a one-time treatment or as a small number of treatments given at widely spaced intervals. This is substantially different to current treatment models for chronic diseases where regular treatment enables annual charging. We may have only limited opportunities to sell our treatment on a patient-by-patient basis, limiting our opportunities to generate revenues. We will therefore need to generate new pricing strategies and business models based on one-time treatments or a very small number of treatments. There can be no assurance that those responsible for reimbursement, government and health administration authorities, private health insurers, managed care programs and other third-party payers, will be receptive to such strategies and models.

### We may become exposed to costly and damaging product liability claims and may not be able to maintain sufficient product liability insurance to cover these claims.

Our business is exposed to potential product liability and professional indemnity risks which are inherent in the research, development, manufacturing, marketing and use of medical treatments and products. It is always possible that a product, even after approval, may exhibit unforeseen failures or side effects. It is impossible to predict the potential adverse effects that our products may have on humans. We face the risk that the use of our products in clinical trials will result in adverse effects, or that long-term adverse effects may only be identified following clinical trials and approval for commercial sale. In addition, there can be no assurance that physicians and patients will comply with any warnings that identify the known potential adverse effects and any patients who should not receive our products.

We have clinical trial and other liability insurance, which we currently believe is adequate to cover liabilities we may incur. However, our current or future insurance coverage may prove insufficient to cover any liability claims brought against us. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for our products. 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.

Some of our collaboration 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.

If we cannot adequately protect ourselves against potential liability claims, we may find it difficult or impossible to commercialize our products.

# Interrupted product supply or development as a result of an unforeseen event may delay and/or damage our ability to generate revenues and our likelihood of success will be harmed.

We may not be able to continue development of our products or obtain certain resources from third parties which we need for the development of our products and we ourselves may not be able to develop our products as a result of an unforeseen event, such as an event of force majeure, a defect in a manufacturing process, a regulatory action, a supply interruption or an adverse change to a supplier agreement.

All of our facilities are located within a single facility in Amsterdam, 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.

# Our products are based on a single underlying technology based on gene therapy using adeno-associated viral vectors.

Our products allow for the specific delivery of therapeutic genes into the nucleus of target cells of patients by packaging them into protein shells (capsids) that are called "vectors". Our vectors are based on the capsid proteins of adeno-associated viruses (AAV), a type of virus which commonly infects humans without causing disease. None of our products based on this technology have been approved by the relevant regulatory authorities and it is not yet certain that our technology will meet the applicable safety and efficacy standards of the regulatory authorities.

For example, the use of AAV vectors for gene therapy has been shown to induce a mild immune response in some patients in clinical trials and scientific work of research institutions, universities and other commercial entities. Our product Glybera® incorporates a regimen of mild immuno-suppression with approved and well-documented agents, which we expect to be sufficient to prevent such immune responses. However, if public perception is influenced

by adverse immunogenic events in the trials and scientific work of others, this product may not be accepted by the general public or the medical community.

Also, if Glybera® is not approved for marketing by the EMA, that may have an adverse affect on acceptance of our other products by the general public or the medical community.

Our success depends substantially on our most advanced products, which are either still in the registration process or in clinical and pre-clinical development. If we are unable to bring these products to market, or experience significant delays in doing so, our ability to generate product revenue and our likelihood of success will be harmed.

The successful development of our products may not be feasible or may be delayed due to various factors including those mentioned hereafter. In addition, regulatory approval, if obtained, could at any time be adversely affected by adverse safety, efficacy or other development data.

In general, any of our products 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 approvals;
- does not offer therapeutic or other improvements (e.g. lower costs or improved patients' convenience) over existing or future drugs used to treat the same conditions;
- is not accepted in the medical community or by third-party payers; or
- is not capable of being produced in commercial quantities at acceptable costs.

Our most advanced product, Glybera® for treatment of LPLD is in the registration process before EMA. Our other products are in various stages of clinical and pre-clinical research. We do not expect any of our current products (including Glybera®) to be commercially available until 2011 at the earliest, if at all. The results of our research, pre-clinical and clinical trials to date cannot provide assurance that acceptable safety or efficacy will be shown upon completion of subsequent clinical trials.

If we are not successful or are significantly delayed in commercializing Glybera® for LPLD, we would be forced to rely on the development of other products.

#### Only one product using baculovirus production technology has as yet been approved.

All our products may be produced in our baculovirus based production system in insect cells. To date, no products have been approved for sale in the EU, the US or any other jurisdiction based on this production platform. Moreover, to our knowledge, only one product using a baculovirus based production system has been approved by the EMA or the FDA for final regulatory approval. If unforeseen technological, regulatory or other challenges associated with this production system or our own production platform materialize, our ability to develop and commercialize our products will be severely disrupted.

We have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future. We may never become profitable.

We have thus far incurred losses in each year since incorporation. Our increasing net loss for the years ended 31 December 2009, 2008 and 2007 amounted to €17.2 million, €16.9 million and €14.9 million, respectively. These losses have arisen mainly from costs incurred in research and development of our products and general and administrative expenses.

We do not currently have any products that have been approved for marketing, and we continue to incur research and development and general and administrative expenses related to our operations. Consequently, we expect to continue to incur losses for at least the foreseeable future as the expansion of our operations and continued development of our products will require substantial marketing, sales, research and development expenditures.

The Company has not paid any dividends since its incorporation. Even if future operations lead to significant levels of distributable profits, of which there can be no assurance, it is at present intended that any earnings will be reinvested in our business and that dividends will not be paid until we have an established sufficient income to support continuing dividends.

Due to our limited operating history and limited experience in the commercial exploitation of our technologies, no assurance can be given that we will achieve profitability in the future. Furthermore, if our products fail in clinical trials or do not gain regulatory approval, or if our products 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 rely on third parties for pre-clinical development activities, clinical trials and to support our regulatory submissions. If these third parties do not perform as contractually required or expected, we may not be able to develop, obtain regulatory approval for or commercialize our products.

We rely partly on third party organizations to conduct our pre-clinical development activities and clinical trials, such as the Center for Applied Medical Research (Centro de Investigación Médica Aplicada - CIMA), a research consortium founded by the University of Navarra, Spain, and St Jude Children's Research Hospital in Memphis, Tennessee, USA (see also "Business - Strategic partnerships"). As a result, we have had, and will continue to have, less operational control over the conduct of such activities and trials, the timing and completion of such activities and trials, the required reporting of adverse events and the management of data developed through such activities and trials than would be the case if we relied entirely upon our own staff. Outside parties may have staffing difficulties, may undergo changes in priorities or may become financially distressed, adversely affecting their willingness or ability to conduct our trials. As a result we may experience unexpected cost increases that are beyond our control. Problems with the timelines or quality of the work of a third party organization, such as a pre-clinical or clinical research organization, may lead us to seek to terminate the relationship and use an alternative service provider. However, making this change may be costly and may delay our pre-clinical development activities and clinical trials. and contractual restrictions may make such a change difficult or impossible. It may be impossible to find a replacement organization that can conduct our pre-clinical development activities and clinical trials in an acceptable manner and at an acceptable cost. Furthermore, if these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons, our pre-clinical development activities or clinical trials may be extended, delayed, suspended or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our products.

#### We are dependent on third party supply of certain goods and services

Our research and development activities are partly dependent on third party supply of goods and services. In addition, there are materials incorporated in our production platform and our products under development which are sourced from third parties. Because of the highly specialized nature of our activities and operations, the choice of eligible suppliers may be

limited, in certain occasions even to a single supplier. Any disruption in the supply of these goods and services could be harmful to our business.

## We rely on the skills and expertise of our key personnel and secondees, and our future depends on our ability to attract and retain qualified personnel.

Our success will depend to a significant degree upon the continued services of key management, technical and scientific personnel and secondees and on our ability to attract and to retain other highly skilled personnel. Whilst we have entered into employment arrangements with our key management, technical and scientific personnel (and in some instances, have entered into secondment or consultancy agreements) with the aim of securing their services and have endeavored to ensure that our employees receive suitable incentives, the retention of their services cannot be guaranteed and our management and other employees may voluntarily terminate their employment with us at any time with short notice. There is intense competition for skilled personnel and the retention of such personnel or secondees or the recruiting of new highly qualified employees on acceptable terms cannot be guaranteed. The loss of such key personnel or secondees or the failure to attract new highly qualified and experienced employees could have a material adverse effect on our business, financial condition and the results of our operations.

Due to our wide ranging activities covering molecular biology, expression technology, protein chemistry and enzymology, assay development, viral vector research, pre-clinical, and clinical development, we have only a limited number of experts in each field. Should one of these experts decease, become (permanently) disabled, leave us or decide to stop cooperating with us, this could have a material negative impact on our operations.

Although the Board of Management and Senior Management, and specifically our Chief Executive Officer, Chief Financial Officer and Director Operations & Project Management, are experienced in the management of biotechnology companies, our future commercial success will depend on our ability to build-up a specialized medical service team with the requisite medical and technical skills to educate and support the treating physicians as well as to negotiate the pricing of the products with the different third-party payers. Our products are high-tech in nature and we therefore believe it is necessary to employ people with scientific expertise and relevant experience in the areas of gene therapy, therapeutic gene identification, clinical development and production in order to successfully commercialize our future products. Failure to attract or to retain sufficient qualified people could have a material adverse effect on our business, financial condition and the results of our operations.

In addition, we may have to rely on consultants and advisors, including scientific and clinical advisors, to assist us due to a temporary lack of personnel. Such 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 rely on collaborative relationships to further develop our business and if we or any of our current or future collaborators fail to perform or terminate any obligations under our collaborative arrangements, our products could be delayed or terminated.

A material component of our business strategy is to establish and maintain collaborative arrangements with pharmaceutical and biotechnology companies, research institutions and foundations and private and public universities for research and development. Currently we have entered into collaboration arrangements with amongst others the Center for Applied Medical Research and St Jude Children's Research Hospital (see also "Business – Strategic partnerships").

We may be unable to locate, and enter into favorable agreements with, suitable third parties, which could delay or impair our ability to develop and commercialize products and could increase our costs of development and commercialization. Furthermore, the reliance on collaboration or partnering arrangements may partially place the development of our products outside our control. This exposes us to a number of risks, including but not limited to the risks that:

- we may not be able to control the amount and timing of resources that our collaborators/partners devote to the product development program;
- our collaborators may experience financial difficulties;
- we may be required to relinquish important rights such as marketing and distribution rights;
- business combinations or significant changes in a collaborator's/ or partner's business strategy may also adversely affect a collaborator's or partner's willingness to complete its obligations under any arrangement;
- a collaborator or partner could move forward with a competing product developed either independently or in collaboration with others, including our competitors; or
- collaboration and partnering arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our products.

### We may fail to select or capitalize on the most scientifically, clinically or commercially promising or profitable products.

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

#### We may encounter difficulties in managing future growth.

Our success will depend on the expansion of our operations and the effective management of growth, which will place a significant strain on our management, operational and financial resources. To manage such growth, we must expand our facilities, augment our operational, financial and management systems and hire and train additional qualified personnel, all of which may lead to significant costs and may divert our management and business development resources.

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

Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the internet, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions in our

collaborations with our partners and delays in our research and development work. These operations may have an adverse effect on our business, financial condition and/or results of operations and could negatively affect the price of our shares. Furthermore failures within our information technology systems may lead regulatory authorities to withhold or suspend the development, registration or commercialization of our programs and products.

#### Exchange rate fluctuations could negatively affect our financial condition.

We are based in the Netherlands but source research and development, consulting and other services from several countries. We also pay and might receive royalties in different currencies and potential future revenue may be derived from abroad, particularly from North America. As a result, our business and share price will be affected by fluctuations in foreign exchange rates between the Euro and other currencies, especially the US and Canadian Dollar, the British Pound and the Swiss Franc which may have a significant impact on our reported results of operations and cash flows from year to year.

#### Risks related to our shares, including the New Shares

The ownership of our shares is highly concentrated with a small number of shareholders who may be in a position to exert significant influence over our management and operations and whose interests may conflict with those of other shareholders

Apparent from the AFM kept public register, there are currently four shareholders which have a share interest of 5% or more. Collectively, these shareholders, all private equity investors, presently own approximately 54% of our shares (see "Major Shareholders"). Some of these shareholders, acting together, may have the ability to exert significant influence over our management and operations, including the election of our Board of Management and other matters submitted to our shareholders for approval pursuant to Dutch law.

The voting power of these shareholders may discourage or prevent certain take-overs or changes in control over us unless the terms are approved upfront by such existing shareholders. These shareholders may vote in a way which our other shareholders do not agree and 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.

### The price of our shares may be volatile and affected by a number of factors, some of which are beyond our control.

The price of shares listed on stock markets can experience wide fluctuations due to various factors including a company's operating results, changes in estimates by stock market analysts, general economic conditions and other events and factors outside a company's control.

Particularly, the markets in which we operate are directly affected by many national and international factors that are beyond our control. Any one of the following factors, amongst others, may cause a substantial decline in the markets in which we operate: legislative and regulatory changes; economic and political conditions; concerns about terrorism and war; the level and volatility of equity and other markets; the level and volatility of interest rates and foreign currency exchange rates; concerns over inflation and changes in institutional and consumer confidence levels. Any of these factors could have an adverse effect on the price of our shares.

Furthermore, securities markets and in particular shares of biopharmaceutical and pharmaceutical companies whose products have not yet been commercialized have

experienced significant price and volume fluctuations in recent years. Such fluctuations in the future could adversely affect the market price for the shares irrespective of our results of operations or financial condition.

#### The volume of trading in our shares has historically been low.

Because of the significant concentration and related limited free float of our shares, the average daily trading volumes of our shares has historically been low, which has resulted and may continue to result in an adverse effect on the liquidity, marketability and market price for our shares.

### The price and trading volume of our shares could decline depending on market appraisal.

The trading market for our shares is 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 or change their recommendation regarding our shares adversely, the market price for our shares and trading volume 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 for our shares or trading volume to decline.

Furthermore, the market price for our shares may fall in response to market appraisal of our strategy or if our operating results and prospects from time to time are below the expectations of market analysts and investors.

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

We do not intend to pay any dividends for the foreseeable future and our ability to pay dividends in the long run is uncertain. Payment of future dividends, if any, to shareholders will effectively be at the discretion of the Board of Management, 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 the 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.

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

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

### **Important Information**

No person is or has been authorized to give any information or to make any representation other than those contained in this Prospectus and, if given or made, such information or representations must not be relied upon as having been authorized by us. Without prejudice to any obligation to publish any supplementary documents pursuant to section 5:23 of the Financial Supervision Act, the delivery of and information in this Prospectus shall not under any circumstances create any implication that there has been no change in our affairs or that information contained herein is correct and complete as of any time subsequent to the date hereof.

Amsterdam Molecular Therapeutics (AMT) Holding N.V. accepts responsibility for the information contained in this Prospectus. To the best of our knowledge and belief (having taken all reasonable care to ensure that such is the case), the information contained in this Prospectus is in accordance with the facts and does not omit anything likely to affect the import of such information.

The information included in this Prospectus reflects our position at the date of this Prospectus and under no circumstances should the issue and distribution of this Prospectus after the date of its publication be interpreted as implying that the information included herein will continue to be correct and complete at any later date.

This Prospectus is to be read in conjunction with all the documents which are incorporated herein by reference (see "Important information - Documents incorporated by reference").

#### **Notice to investors**

The distribution of this Prospectus may be restricted by law in certain jurisdictions and therefore persons into whose possession this document comes should inform themselves of and observe any such restrictions.

The New Shares have not been and will not be registered under the Securities Act or under any securities laws of any state or other jurisdiction of the United States and may not be taken up, offered, sold, resold, transferred, delivered or distributed, directly or indirectly, in or into or from the United States except pursuant to an applicable exemption from, or in a transaction not subject to, the registration requirements of the Securities Act and in compliance with the securities laws of any state or other jurisdiction of the United States.

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 authorities passed upon or endorsed the merits of any offering of our shares 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.

Unless otherwise indicated, all references in this Prospectus to "€", "Euro", "Eur", "EUR" or "cents" are to the currency introduced at the start of the third stage of the European economic or monetary union pursuant to the treaty establishing the European Community, as amended. All references to "\$", "US\$", "USD" or "US dollars" are to the lawful currency of the United States.

Our consolidated financial statements for the financial years ended 31 December 2009, 2008 and 2007 incorporated by reference in this Prospectus have been audited by PricewaterhouseCoopers Accountants N.V., independent auditors, as stated in its auditor's reports thereon which are also incorporated by reference in this Prospectus.

Our unaudited consolidated interim financial report for the six months ended 30 June 2010 incorporated by reference in this Prospectus has been reviewed by PricewaterhouseCoopers Accountants N.V., independent auditors, as stated in its review report thereon which is also incorporated by reference in this Prospectus.

#### Documents incorporated by reference

The Company's articles of association (*statuten*) as they read on the date of this Prospectus (the "**Articles of Association**") are incorporated by reference in this Prospectus. In addition, the following parts of our audited annual reports for the years 2009, 2008 and 2007 and our unaudited condensed interim financial report for the six months ended 30 June 2010 are incorporated by reference into this Prospectus:

#### Annual report 2009

- Consolidated balance sheet page 56
- Consolidated income statement page 57
- Consolidated statement of comprehensive income page 58
- Consolidated statement of changes in equity page 59
- Consolidated cash flow statement page 60
- Notes to the consolidated financial statements pages 61 through 91
- Auditor's report pages 98 and 99

#### Annual report 2008

- Consolidated balance sheet page 30
- Consolidated income statement page 31
- Consolidated statement of changes in equity page 32
- Consolidated cash flow statement page 33
- Notes to the consolidated financial statements pages 34 through 68
- Auditor's report pages 76 and 77

#### Annual report 2007

- Consolidated balance sheet page 54
- Consolidated income statement page 55
- Consolidated statement of changes in equity page 56
- Consolidated cash flow statement page 57
- Notes to the consolidated financial statements pages 58 through 93
- Auditors' report pages 100 and 101

Condensed interim financial report for the six months ended 30 June 2010

- Consolidated balance sheet page 8
- Consolidated income statement page 9
- Consolidated statement of comprehensive income page 10
- Consolidated statement of changes in equity page 11
- Consolidated cash flow statement page 12
- Selected notes to the condensed interim financial report pages 13 through 20
- Auditors' report page 22

Where the documents incorporated by reference themselves incorporate information by reference, such information does not form part of this Prospectus.

Prospective investors should rely only on the information that we incorporate by reference or provide in this Prospectus. No other documents or information, including the content of our website - www.amtbiopharma.com - or of websites accessible from hyperlinks on our websites, form part of, or are incorporated by reference into, this Prospectus.

Copies of our annual reports for the years 2009, 2008 and 2007, our unaudited condensed interim financial report for the six months ended 30 June 2010, the Articles of Association and this Prospectus may be obtained free of charge for a period of twelve months following the date of this Prospectus by sending a request in writing to us at our business address: Meibergdreef 61, 1105 BA Amsterdam Zuidoost, the Netherlands (tel.: +31 20 566 7394, e-mail: info@amtbiopharma.com) and are also available via www.amtbiopharma.com.

#### **Enforceability of judgments**

Amsterdam Molecular Therapeutics (AMT) Holding N.V. is a public limited liability company (naamloze vennootschap) incorporated under the laws of the Netherlands. Most of our employees and Board of Management, Supervisory Board and Senior Management members are residents outside of the United States and all our assets and, as far as we are aware, a substantial portion of 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

We have used data sources and publications form third parties in relation to certain matters noted in this Prospectus. Such 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. 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.

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

#### **Forward-looking statements**

This Prospectus contains certain statements that are or may be forward-looking statements with respect to our financial condition, results of operations and/or business achievements, including, without limitation, statements containing the words "believe", "anticipate", "expect", "estimate", "may", "could", "should", "would", "will", " intend" and similar expressions. Such forward-looking statements involve unknown risks, uncertainties and other factors which may cause our actual results, financial condition, performance or achievements, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed described under "Risk Factors" beginning on page 10 of this Prospectus. Given these uncertainties, prospective investors are cautioned not to place any undue reliance on such forward-looking statements. We disclaim any obligation to update any such forward-looking statements in this Prospectus to reflect future events or developments.

#### References to defined terms and incorporation of terms

Certain terms used in this Prospectus, including capitalized terms and certain technical and other terms are explained in the section entitled "Definitions and Glossary".

### **Dividends and Dividend Policy**

#### General

We may only make distributions to our shareholders in so far as our shareholders' equity exceeds the aggregate of our paid-in and called-up share capital plus the reserves, as required to be maintained by Dutch law or by the Articles of Association.

The Board of Management 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 shares.

Under the Articles of Association, we may only make a distribution of dividends to our shareholders after adoption of our annual accounts demonstrating that such distribution is legally permitted. With the approval of the Supervisory Board, and with due observance of applicable law, the Board of Management may declare an interim dividend on the shares.

#### Manner of dividend payment

The General Meeting of Shareholders may, at the proposal of the Board of Management, which proposal is subject to approval by the Supervisory Board, resolve that a distribution of dividends on the shares shall not be paid in whole or in part in cash, but in shares.

The date on which dividends and other distributions shall be made payable shall be announced by means of a publication on our website.

Unless the General Meeting of Shareholders determines another date of payment, dividends and other distributions shall be made payable immediately after they have been declared.

Claims to dividends and other distributions not made within five years from the date that such dividends or distributions became payable, will lapse (*verjaren*) and any such amounts will be considered to have been forfeited to us.

#### Dividend ranking of shares

Each of our shares entitles its holder to equal ranking rights to dividends and other distributions.

#### **Dividend history**

The Company has not paid any dividends since its incorporation.

#### **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.

#### **Taxation on dividends**

We are generally required to withhold Dutch dividend withholding tax at a rate of 15% from dividends distributed by us. See "Taxation" for more details and information on Dutch taxation aspects in relation to dividends or distributions.

#### **Use of Proceeds**

We intend to raise up to of €16.3 million in gross proceeds in the Private Placement. Based on gross proceeds of €16.3 million, the costs of the Private Placement are expected to amount to approximately €1.3 million, resulting in expected net proceeds of approximately €15 million.

We intend to use the net proceeds of the Private Placement primarily for general corporate purposes, including:

- furthering the regulatory process of Glybera® for Lipoprotein Lipase Deficiency and, if marketing approval is obtained, commercialization of Glybera® for Lipoprotein Lipase Deficiency, including building our specialist marketing and sales team should we decide to market Glybera® ourselves (see also "Business Products and product pipeline Glybera® for Lipoprotein Lipase Deficiency");
- development activities for AMT-080 for Duchenne Muscular Dystrophy, including the scheduled Phase I/II trials;
- development activities for AMT-060 for Hemophilia B, including clinical trials and further studies to progress this program through the clinical phase;
- development activities for AMT-021 for Acute Intermittent Porphyria, including preclinical and clinical development studies;
- development activities for AMT-090 for Parkinson's Disease, including preclinical and clinical development studies; and
- other general corporate purposes, including working capital requirements, capital expenditures and acquisitions if and when they present themselves.

This intended use of the net proceeds of the Private Placement represents our current intentions based upon our present plans and business conditions. The amounts and timing of our actual expenses depend on numerous factors, including the further course and outcome of the EMA review of our application for marketing authorization for Glybera® for LPLD, the course and outcome of the intended filing for market approval in Canada and the United States, the manner in which we define, implement and execute our commercialization strategy for Glybera® for LPLD, the ongoing status of and results from clinical trials and other studies for our products, as well as the development of our pre-clinical product portfolio and research being carried out, any collaborations that we may enter into with third parties for our products and any unforeseen cash needs. As a result, the Board of Management will retain broad discretion over the allocation of the net proceeds of the Private Placement.

### **Capitalization and Indebtedness**

This section sets forth our unaudited consolidated cash and cash equivalents, capitalization and indebtedness as of 31 August 2010 on an actual basis.

The financial information in the table below has been derived from our 31 August 2010 management accounts which have not been audited or reviewed and which will not be published. You should read this table together with our unaudited condensed consolidated interim financial statements as at and for the six months ended 30 June 2010 and the related notes thereto incorporated by reference in this Prospectus and our audited consolidated financial statements as at and for each of the years ended 31 December 2009, 2008 and 2007 and the related notes thereto incorporated by reference in this Prospectus, as well as the information under "Operating and Financial Review".

€ in thousands	31 August 2010 Unaudited		
Cash and cash equivalents	11,284		
Share capital Share premium Retained earnings Other reserves	595 86,094 (82,097) 831		
Total equity	5,423		
Current liabilities Non-current liabilities <sup>(1)</sup>	4,573 5,872		
Total liabilities <sup>(2)</sup>	10,445		
Total equity and liabilities	15,868		

- (1) Included in the non-current liabilities is an amount of €4,772,500 in relation to the convertible loan notes we issued on 22 December 2009 (see also "Description of Share Capital Convertible loan notes"). For further information, see also note 7 (Non-current liabilities) of the selected notes to the unaudited condensed interim financial report for the six months ended 30 June incorporated by reference in this Prospectus.
- (2) None of the liabilities shown in the above table are secured or guaranteed. For completeness sake we note that to the extent they shall become repayable, funds received under the innovation credit from the Dutch government (SenterNovem) for the development of our treatment for Duchenne Muscular Dystrophy shall be secured by a right of pledge (see also "Operating and Financial Review Contractual obligations").

See "Operating and Financial Review – Contractual obligations" for information on certain of our contingent obligations.

As of 31 August 2010, the Company's authorized capital amounted to €1,000,000 divided into 25,000,000 shares with a nominal value of €0.04 each. Pursuant to an amendment of its articles of association on 29 September 2010 the Company's authorized capital was increased to €1,300,000 divided into 32,500,000 shares with a nominal value of €0.04 each. The Company's issued and outstanding share capital as of 31 August 2010 amounted to € 595,549.12 consisting of 14,888,728 shares with a nominal value of €0.04 each, all fully paid up and created under Dutch law.

#### **Selected Financial Information**

The selected consolidated financial information set forth below should be read in conjunction with "Operating and Financial Review" and our audited consolidated financial statements and notes thereto and our unaudited condensed interim financial report parts of which are incorporated by reference in this Prospectus.

The selected consolidated financial information has been extracted from our annual consolidated financial statements for the years ended 31 December 2009, 2008 and 2007 that have been audited by PricewaterhouseCoopers Accountants N.V., independent auditors, and from our unaudited condensed interim financial report for the six months ended 30 June 2010.

Our consolidated financial statements, from which the selected consolidated financial information set forth below has been derived, were prepared in accordance with IFRS, as endorsed by the European Union. The consolidated interim report has been prepared in accordance with IAS 34 'Interim Financial Reporting' and, as allowed under IAS 34, it does not contain all information required to be included in the financial statements. It should therefore be read in conjunction with the consolidated financial statements for the year 2009.

Our selected consolidated financial information set out below may not contain all of the information that is important to you.

#### Consolidated income statement data

	6 months ended 30 June		Year ended 31 December		
(€ in thousands)	2010	2009	2009	2008	2007
,	unaudited				
Other income <sup>(1)</sup>	563	85	355	223	110
Total net income	563	85	355	223	110
Research and development costs	(8,128)	(7,070)	(13,241)	(13,118)	(9,804)
General and administrative costs	(1,796)	(2,914)	(4,913)	(5,895)	(4,966)
Total operating costs	(9,893)	(9,984)	(18,154)	(19,013)	(14,770)
Operating result	(9,330)	(9,899)	(17.799)	(18,790)	(14,660)
Interest income Interest costs	168 (189)	488 (12)	647 (23)	1,901 (30)	1,406 (1,681)
	(21)	476	624	1,871	(275)
Result before corporate income taxes	(9,351)	(9,423)	(17,175)	(16,919)	(14,935)
Corporate income taxes Result for the	- (9,351)	- (9,423)	- (17,175)	- (16,919)	- (14,935)
	(0,00.)	(-,,	· ····································	( , )	(, )

period					
Attributable to shareholders of the Company	(9,351)	(9,423)	(17,175)	(16,919)	(14,935)

<sup>(1)</sup> Our other income comprises grant revenues. See also "Operating and Financial Review – Material factors affecting our results of operations and financial condition – Other income".

#### Consolidated balance sheet data

	As at 30 June		As at 31 December			
(€ in thousands)	2010	2009	2009	2008	2007	
ACCETO	unaudited					
ASSETS						
Non-current assets						
Intangible assets Property, plant and	2,917 1,541	2,497 2,048	3,008 1,756	2,497 2,338	1,897 2,102	
equipment	,-	, -	,	,	, -	
	4,458	4,545	4,764	4,835	3,999	
Current assets Receivables from related parties	58	-	34	44	985	
Social security and other taxes	285	160	414	102	714	
Other receivables	501	671	469	1,048	1,211	
Cash and cash equivalents	13,511	25,032	22,624	34,150	51,330	
	14,355	25,863	23,541	35,344	54,240	
Total assets	18,813	30,408	28,305	40,179	58,239	
EQUITY Shareholders'	9,108	25,682	18,410	35,105	51,407	
equity <b>Total group equity</b>	9,108	25,682	18,410	35,105	51,407	
LIABILITIES Non-current liabilities						
Financial lease	215	300	259	341	402	
Other non-current liabilities	4,848	-	4,723	110	604	
	5,063	300	4,982	451	1,006	
Current liabilities Trade payables Payables to related	1,558 -	738 -	1,182 -	1,178 219	2,168 730	
party Social security and other taxes	496	215	215	154	227	
Other current liabilities	2,588	3,473	3,516	3.072	2,701	

	4,642	4,426	4,913	4,623	5,826
Total liabilities	9,705	4,726	9,895	5,074	6,832
Total equity and	18,813	30,408	28,305	40,179	58,239
liabilities					

## **Consolidated cash flow statement**

(€ in thousands)	6 months er 2010	nded 30 June 2009	Year ended 31 December 2009 2008 2007			
	unau	ıdited				
Cash flow from operating activities						
Result before corporate income tax adjustments for:	(9,351)	(9,423)	(17,175)	(16,919)	(14,935)	
<ul><li>Depreciation</li><li>Impairment of intangible assets</li></ul>	344 300	347 -	688 -	653 -	334 -	
- Share-based payment expenses	26	(17)	440	(266)	1,143	
- Changes in working capital	(242)	32	165	517	1,003	
- Interest (income)/expense	21	(488)	(624)	(1,871)	275	
Net cash generated from operating activities	(8,902)	(9,549)	(16,529)	(17,888)	(12,180)	
Cash flow from investing activities						
Purchases of property, plant and equipment	(129)	(57)	(106)	(889)	(1,345)	
Purchases of intangible fixed assets	(209)	-	(511)	(600)	(357)	
Interest received	104	488	857	1,901	1,406	
Net cash used in investing activities	(234)	431	240	412	(296)	
Cash flow from financing activities						
Redemption of loans Capital contribution shareholders	23	-	- 40	- 296	(1,613) 51,361	
Convertible loan draw down, net costs	-	-	4,723	-	-	
Net cash generated from financing activities	23	-	4,763	296	49,748	
Net (decrease)/increase	(9,113)	(9,118)	(11,526)	(17,180)	37,272	

in cash, cash equivalents and bank overdrafts					
Cash, cash equivalents and bank overdrafts in the beginning of the period	22,624	34,150	34,150	51,330	14,058
Cash, cash equivalents at the end of the period	13,511	25,032	22,264	34,150	51,330

# **Operating and Financial Review**

The following information, discussion and analysis of our consolidated results of operations and financial condition should be read in conjunction with the whole of this Prospectus, including our audited consolidated financial statements and notes thereto and our unaudited condensed interim financial report which are incorporated by reference in this Prospectus, and (ii) "Selected Consolidated Financial Information".

This information, discussion and analysis contains forward-looking statements that are subject to known and unknown risks and uncertainties. Our actual results and the timing of events could differ materially from those expressed or implied by such forward-looking statements as a result of various factors, including those discussed below and elsewhere in this Prospectus, including under the headings "Forward-Looking Statements" and "Risk Factors". We do not undertake any obligation to revise, or publicly release the results of any revision to, these forward-looking statements.

#### Overview

Founded in 1998 and based in Amsterdam, we are a leader in the development of human gene based therapies. Using Adeno Associated Virus (AAV) as the delivery vehicle of choice for therapeutic genes, we have been able to design and validate what is probably the first stable and scalable AAV production platform. This safe and efficacious proprietary platform offers a unique manufacturing capability which can be applied to a large number of rare (orphan) diseases that are caused by one faulty gene. In addition, the AAV delivery vehicle has the potential to be developed as a delivery system into cells for other therapeutic molecules, making it an intra-cellular delivery system. This increases the potential range of applications.

Currently, we have a product pipeline with several AAV-based gene therapy programs for Lipoprotein-Lipase Deficiency (LPLD), Duchenne Muscular Dystrophy (DMD), Hemophilia B, Acute Intermittent Porphyria (AIP) and Parkinson's Disease (PD) at different stages of research or development.

In our early years we were funded by the AMC, government grants, and from income derived from cGMP contract manufacturing of biologics for third parties. In July 2006, we raised €22 million in a private financing round with a group of venture capital investors. In June 2007, we completed our initial public offering and our shares were admitted to listing and trading on Euronext Amsterdam, raising an additional €56 million. In December 2009, we strengthened our financial position via a private placement of convertible loan notes to funds associated with Forbion Capital Partners, raising €5 million. In January 2010, we were granted an innovation credit from the Dutch government for the development of our treatment for Duchenne Muscular Dystrophy.

### Material factors affecting our results of operations and financial condition

We believe that the factors discussed in the following paragraphs have had or are expected to continue to have a material effect on our operational results and financial condition. Reference is also made to "Operating and Financial Review - Outlook" and, given the fact that our business is subject to extensive government regulation, to "Business – Government regulation and product approval".

#### Other income

Our other income during the entire period covered by the historical financial information included in this Prospectus represents our total net income during such period.

Our other income comprises grant revenues. To date the majority of these grants have been received from the Dutch Ministry of Economic Affairs and from the European Union (see also "Operating and Financial Review – Contractual obligations"). Going forward we expect to continue to be able to fund part of our programs through existing and newly acquired grants.

### Operating costs

Our operating costs currently consist of two categories: research and development, and general and administrative costs.

All our research and development costs during the entire period covered by the historical financial information included in this Prospectus are related to pre-clinical and clinical development (including registration activities) and earlier stage research. Research and development costs comprise, amongst others, allocated employee costs, cGMP facility costs, clinical development costs, collaboration costs, license costs, the costs of laboratory consumables and allocated depreciation costs. The allocation of employee costs is based on the nature of the work the employees are carrying out.

General and administrative costs comprise allocated employee costs, office costs, consultancy costs, allocated depreciation costs and administrative costs.

The main factors affecting our operating costs are:

- the development phase of the various programs in our pipeline and the extent to which development is carried out by third parties – in particular, later stage clinical studies typically require treatment of progressively larger numbers of patients and therefore tend to be increasingly expensive;
- the costs of third party supply of research and development related goods and services; and
- our headcount and employee benefit and other personnel costs.

### Summary of operational and financial results

### Six months ended 30 June 2010 compared to six months ended 30 June 2009

#### Revenues

Our other income – consisting of grant revenues - increased to €0.6 million for the six month period ended 30 June 2010 from €0.1 million in the same period of 2009. In relation to the six month period ending 30 June 2010, €0.4 million was received under the investment credit (*innovatiekrediet*) which we were granted by the Dutch government for the development of our Duchenne Muscular Dystrophy program (see also "Operating and Financial Review – Contractual obligations").

### Operating costs

The main item within operating costs reflects the investment in Glybera® for LPLD to support the EMA registration process (which is described more fully in "Business – Programs and pipeline - Glybera® for Lipoprotein-Lipase Deficiency).

We continued the development of our Duchenne Muscular Dystrophy program, which is 35% funded by the above mentioned investment credit. Expenditure on our other development projects was reduced in the first half year of 2010, as we are constrained by our current resources and are focusing on the successful completion of the EMA registration process of Glybera® for LPLD.

Research and development costs increased to €8.1 million for the six month period ended 30 June 2010 from €7.1 million in the same period of 2009. The research and development costs included a €0.3 million write-off of a previously capitalized intangible asset as a consequence of a terminated research and license agreement. General and administrative costs decreased to €1.8 million in the six month period ended 30 June 2010 from €2.9 million in the same period of 2009, which earlier period included certain non-recurring expenses.

#### Interest

Net interest income/(cost) decreased to €(0.0) million for the six month period ended 30 June 2010 from €0.5 million in the same period in 2009 as a result of our decreasing cash balance, combined with continuing low market interest rates for deposits, and interest accruing on the €5.0 million convertible loan issued by us in December 2009.

### Result for the period

Total net loss for the six month period ended 30 June 2010 amounted to €9.4 million, in line with the net loss for the six month period ended 30 June 2009 which also amounted to €9.4 million. The loss per share amounted to €0.63 for the six month period ended 30 June 2010 compared to €0.64 for the six month period ended 30 June 2009. The basic and diluted loss per share are the same because we were loss-making in both periods.

### Cash flow and cash position

Cash and cash equivalents amounted to €13.5 million at 30 June 2010, a decrease of €9.1 million compared to €22.6 million at 31 December 2009. The decrease in cash and cash equivalents mainly stems from the operational cash outflow which amounted to €8.9 million for the period ended 30 June 2010 (compared to an operating cash outflow of €9.5 million for the period ended 30 June 2009).

#### Equity

Shareholders' equity amounted to €9.1 million at 30 June 2010 compared to €18.4 million at 31 December 2009, the decrease mainly stemming from the contribution of the loss for the period. A total number of 14,888,728 shares were issued and outstanding at 30 June 2010.

### Year ended 31 December 2009 compared to year ended 31 December 2008

### Revenues

The total net income for the year ended 31 December 2009 amounted to  $\le$ 0.4 million, a 100% increase compared to the total net income for the year ended 31 December 2008 which amounted to  $\le$ 0.2 million. These revenues represented grant income from the Dutch government.

### Operating costs

Research and development costs amounted to €13.2 million for the year ended 31 December 2009, broadly in line with the €13.1 million for the year ended 31 December 2008. The general and administrative costs amounted to €4.9 million for the year ended 31 December 2009, a decrease of 17% compared to €5.9 million for the year ended 31 December 2008. This decrease reflected the higher than normal cost of advisory fees in 2008 which did not recur to the same level in 2009. The general and administrative costs were also affected by non-recurring reorganization costs incurred in 2009.

#### Interest

Our interest income - interest earned on our cash deposits on interest bearing accounts - decreased to €0.7 million in the year ended 31 December 2009 from €1.9 million in the year ended 31 December 2008. The interest income mainly stems from interest generated on short term cash deposits. The decrease in interest income reflects the lower average cash balance during 2009 and the persistent low interest rates generally available on deposits.

Interest costs amounted to €0.0 million for the year ended 31 December 2009, in line with the amount of €0.0 million for the year ended 31 December 2008. The interest costs in 2009 mainly related to a small interest charge in relation to the €5 million convertible loan which was drawn down on 23 December 2009, and to finance costs. The convertible loan comprises five-year unsecured and unsubordinated convertible loan notes, which were issued at par and pay an annual coupon of 5%. The convertible loan notes are due 31 December 2014 (see also "Description of Share Capital and Corporate Governance – Convertible loan notes).

### Result for the period

Our operating loss reduced slightly to €17.8 million for 2009, from €18.8 million for 2008.

Total net loss for the year ended 31 December 2009 amounted to €17.2 million, broadly in line with the net loss for the year ended 31 December 2008 which amounted to €16.9 million. The loss per share amounted to €1.17 for 2009 compared to €1.16 for 2008. The basic and diluted loss per share are the same because we are loss-making in both periods.

### Cash flow and cash position

Cash and cash equivalents amounted to € 22.6 million at 31 December 2009, a decrease of 34% compared to €34.2 million at 31 December 2008. The decrease in cash and cash equivalents reflects the net cash outflow which amounted to €11.5 million for the year ended 31 December 2009, compared to a net cash outflow of € 17.2 million in 2008. The outflow in 2009 comprises net cash used in operations of € 16.5 million, compared to € 17.9 million in 2008, the difference mainly stemming from non-recurring reorganization costs made in 2008. Cash flow from financing activities, principally the draw down of the convertible loan, amounted to € 4.8 million, compared to € 0.3 million in 2008. The total net decrease in cash and cash equivalents amounted to € 11.5 million compared to € 17.2 million in 2008.

### Equity

Shareholders' equity amounted to €18.4 million at 31 December 2009 compared to €35.1 million at 31 December 2008, the decrease mainly stemming from the contribution of the loss for the period. A total number of 14,813,728 shares were issued and outstanding at 31 December 2009.

## Year ended 31 December 2008 compared to year ended 31 December 2007

#### Revenues

The total net income for the year ended 31 December 2008 amounted to €0.2 million, compared to a total net income for the year ended 31 December 2007 of €0.1 million. These revenues represent grant income from the Dutch government.

## Operating costs

Our research and development costs amounted to €13.1 million for the year ended 31 December 2008 compared to €9.8 million for the year ended 31 December 2007, an increase of 34%. This increase in costs is mainly a result of the increase in the number of research and development staff, an increase in pre-clinical and clinical activities, especially related to Glybera® for LPLD, and the increase in research collaborations.

Our general and administrative costs amounted to €5.9 million for the year ended 31 December 2008 an increase of 18% compared to €5.0 million for the year ended 31 December 2007. This increase in costs is mainly due to increased employee costs, non-recurring reorganization costs and increased advisory fees.

#### Interest

Interest income - interest earned on our cash deposits on interest bearing accounts - increased to €1.9 million in the year ended 31 December 2008 from €1.4 million in the year ended 31 December 2007.

Interest costs amounted to €0.0 million for the year ended 31 December 2008, compared to an expense of €1.7 million for the year ended 31 December 2007. The interest costs in 2007 were mainly related to two debts: a liability to preference shareholders and a loan from a related party. The liability to preference shareholders was converted into equity at the time of our initial public offering. The loan from the related party was initially valued at a discounted value. However, this loan became repayable upon the initial public offering and had to be revalued. This revaluation has been recognized as interest expense for the year ended 31 December 2007.

### Result for the period

Total net loss for the year ended 31 December 2008 amounted to €16.9 million, an increase of 13% compared to the net loss for the year ended 31 December 2007 which amounted to €14.9 million. The loss per share amounted to €1.16 for 2008 compared to €1.28 for 2007. The basic and diluted loss per share are the same because we are loss-making in both periods.

### Cash flow and cash position

Cash and cash equivalents amounted to €34.2 million at 31 December 2008, a decrease of 33% compared to €51.3 million at 31 December 2007. The decrease in cash and cash equivalents mainly stems from the operational cash outflow which amounted to €17.9 million for the year ended 31 December 2008, compared to €12.2 million in 2007. The increase in operational cash outflow was largely caused by a significant increase in headcount in 2008 as we expanded the scope and range of our activities and was furthermore affected from non-recurring reorganization costs made in 2008.

### Equity

Shareholders' equity amounted to €35.1 million at 31 December 2008 compared to €51.4 million at 31 December 2007, the decrease mainly stemming from the contribution of the loss for the period. A total number of 14,676,545 shares were issued and outstanding at 31 December 2008.

## Liquidity and capital resources

Our main sources of liquidity since our initial public offering in June 2007 have been our funds generated from equity finance (including the issue of convertible securities) and grant finance by government and EU grants. Since 2007 we have expanded our operations to meet the requirements for late stage clinical development and registration of our lead program Glybera® for LPLD and to continue the progression of the other programs in our portfolio.

In the initial public offering in June 2007 we raised €56 million before costs. In December 2009 we issued convertible loan notes for an aggregate amount of €5 million (see "Description of Share Capital and Corporate Governance – Share capital – Convertible loan notes).

### **Principal investments**

The principal investments in the period covered by the historical financial information included in this Prospectus related to investments in intangible assets (intellectual property).

The principal investment in intangible assets during the financial year ended 31 December 2007 regarded the payment and capitalization of a milestone fee of €357,000 related to our sublicense agreement with Targeted Genetics related to AAV1 vector technology. The principal investment in intangible assets during the financial year ended 31 December 2008 regarded the payment and capitalization of licensing fees totaling €600,000 related to a license from the "La Sapienza" University of Rome for technology for treatment for Duchenne Muscular Dystrophy and a license from the "San Rafaelle" University of Milano for technology to be used in the treatment of Hemophilia B. The principal investment in intangible assets during the financial year ended 31 December 2009 regarded the accrual of a licensing milestone of \$750,000 (€511,000) to Targeted Genetics which became payable on the submission of the marketing authorization application of Glybera® for LPLD to the EMA. In the six month period ended 30 June 2010 we terminated a research and license agreement under which we had made an initial payment of €300,000. This payment had been capitalized as an intangible asset, and accordingly this amount has been written off. Reference is made to note 5 (Intangible Assets) of the notes to the audited consolidated financial statements for the years 2009 and 2008 and note 4 (Intangible Assets) of the selected notes to the unaudited condensed interim financial report for the six months ended 30 June 2010 included by reference in this Prospectus for further information.

Other investments in the period covered by the historical financial information related to investments in property, plant and equipment. Such investments in property, plant and equipment regarded items which individually are not material and are all used in the ordinary course of business. Reference is made to note 6 (Property, Plant and Equipment) of the notes to the audited consolidated financial statements for the years 2009 and 2008 included by reference in this Prospectus for further information.

#### **Contractual obligations**

We lease our offices and laboratory space as well as our manufacturing facility and related equipment under various operating and financial lease agreements, mainly:

- an agreement with subsidiaries of the AMC for the lease of a building located on Meibergdreef 61 from 1 October 2005 until 30 September 2016 and an agreement for the lease of Meibergdreef 57 from 1 July 2006 until 30 September 2016. The annual lease payment amounts to €360,000. These contracts contain an option to extend the lease by another five years under similar conditions.
- an agreement with a subsidiary of the AMC regarding leasehold improvements at Meibergdreef 61 as from October 2005 for 11 years. The rent of the leasehold improvements amounts to €30,000 per year. The lease contract contains an option to extend the lease for another five years. We have the right to cancel the lease earlier on a one-year term however, we will then need to repay the remaining amount of leased leasehold improvements.
- an agreement with a subsidiary of the AMC regarding leasehold improvements at Meibergdreef 57 as from July 2006 for 10 years and 3 months. The rent of the leasehold improvements amounts to €23,000 per year. The lease contract contains an option to extend the lease for another five years.

• an asset production agreement with a subsidiary of the AMC regarding certain equipment and other assets as from 12 June 2006 until 31 December 2010. The total payment over the years by us is €319,000. At the end of the lease the legal ownership of these assets transfers to us.

From 1 October 2000 until 31 May 2005, we received a grant called "Technisch ontwikkelingskrediet" (TOK) from the Dutch government. This TOK grant includes a repayment clause in case we generate revenues from this project. We received a total grant of €3,605,000 relating to eligible project costs in the period mentioned. The grant amount received carries an interest of 5.7% per annum and needs to be repaid in the period 1 January 2008 through 31 December 2017 as a percentage of revenues which are derived from the sale of Glybera® for LPLD. If future royalty payments are not sufficient to repay the grant on or prior to 3 December 2017, or if there are no revenues generated, the remaining balance will be forgiven. Repayment obligations continue to apply if the product is not commercialized or transferred to others. The total amount of the liability at 30 June 2010 was €5,207,000 comprising the original total amount of the grant together with accrued interest.

Historically, we also received a "Technisch ontwikkelingsproject" (TOP) grant in relation to a project that was terminated. If we realize income from the sale of assets developed with or under that grant, repayment clauses will apply up to an amount of €130,000.

On 5 January 2010 we were awarded an investment credit (*innovatiekrediet*) from the Dutch government (Ministry of Economic Affairs – Agentschap.nl) in respect of our program for Duchenne Muscular Dystrophy. The credit covers 35% of the costs incurred in respect of the program up to a maximum of €4 million. The credit includes a repayment clause dependent on the technical success of this program. The credit is interest-bearing at a rate of 11.4% per annum. To date we have received €729,000 under this investment credit. At 30 June 2010 no interest had yet accrued in respect of this liability. The grant needs to be repaid after the funded part of the program has completed in 2013 out of a percentage of revenues which are derived from the sales of our Duchenne Muscular Dystrophy program. The assets which are financed by means of the investment credit are subject to a right of pledge for the benefit of the Dutch Ministry of Economic Affairs.

In 2010, together with certain other parties we have formed a consortium that was granted EU funding (under the Seventh Framework Programme for research and technological development (FP7)) relating to the TreatRetUsher project (Fighting blindness of Usher syndrome: diagnosis, pathogenesis and retinal treatment).

In the course of our business we entered into contracts with other parties as a licensee to obtain freedom to operate with regard to the development and commercialization of certain parts of our programs, including licenses covering the vectors, genes and manufacturing processes. These contracts are entered into in the ordinary course of business and certain of the terms of these agreements are commercially sensitive and are not fully disclosed by us. In particular, in certain cases we will need to make milestone payments to the licensors when we reach pre-defined milestones, and we will need to pay royalties to licensors on future sales levels. Because the timing and realization of the pre-defined milestones is uncertain, as are the levels of future sales, the financial effects of these arrangements cannot be estimated reliably.

We have entered into certain research and development commitments in relation to our pipeline, primarily in relation to our program for Acute Intermittent Porphyria.

The following table provides an overview as per 31 December 2009 of our aggregate minimum future payments under our lease commitments and our research and development commitments over the periods indicated.

(€ in thousands)	No later than 1 year	Later than 1 year and no later than 5 years	Later than 5 years	Total
Financial lease	100	317	0	417
Operating lease	698	1,719	426	2,846
Research and development	387	40	0	427

### Off balance sheet arrangements

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

## Working capital statement

Our current cash resources do not provide us with sufficient working capital for the next twelve months following the date of this Prospectus.

We do have sufficient working capital until into the second quarter of 2011. Based on our present requirements we need additional cash resources of approximately €11 million to provide us with sufficient working capital for the next twelve months following the date of this Prospectus. If the Private Placement should be withdrawn or otherwise not be completed, or if the net proceeds raised by means of the Private Placement shall be less than €11 million, we require additional funds to cover the deficit in our working capital for the next twelve months following the date of this Prospectus. In that event we may seek to enter into (i) debt or equity financing arrangements by means of private or public offerings (ii) partner, license or other agreements with pharmaceutical companies or other third parties to obtain milestone, royalty or other payments for one or more programs in our pipeline. We may then also (iii) decrease our operational and capital expenditure by reducing investments in our pipeline or (iv) sell some of our assets, or any combination of those options. In the event we will not be able to generate sufficient funds from these resources, we may be unable to continue as a going concern and our business, financial condition and/or results of operations could be materially and adversely affected.

If the Private Placement is completed and a minimum of €11 million in net proceeds is raised, such net proceeds together with our current cash resources will provide us with sufficient working capital for the next twelve months following the date of this Prospectus. As described in "Private Placement – Private Placement" certain investors have committed to us to subscribe for New Shares for a total amount of €3.75 million.

This working capital statement covers Amsterdam Molecular Therapeutics (AMT) Holding N.V. together with its subsidiaries.

#### Outlook

### Cash position

Our expenditure continues to be in line with budget. We have not yet reached the point of generating revenues that could fund our operations, however. As at 30 June 2010 our cash resources amounted to €13.5 million and as at 31 August 2010 to €11.3 million. Since then, in line with budget and in the ordinary course of business our cash resources have further decreased and are expected to be depleted in the second quarter of 2011 if no additional

cash is received. This matter has also been reflected in the emphasis of matter which is included in the review report to our unaudited condensed interim financial report for the six months ended 30 June 2010 to which reference is made. See also "Operating and Financial Review – Working capital statement".

#### Revenues

First sales of Glybera® for LPLD in a "named-patient-sales" program in France are expected early 2011 (see also "Business – Programs and pipeline - Glybera® for Lipoprotein Lipase Deficiency).

### Research and development costs

Following our initial public offering in 2007, we increased the number of specialized employees who support our pre-clinical and clinical activities. We believe that our current staff levels, which have been broadly stable since 2008, are appropriate to the scale of operations and we have no current plans to significantly change these.

### General and administrative costs

In 2008 and 2009 we incurred certain reorganization costs. These are not expected to recur, and we expect general and administrative costs to continue at current levels. In the event that Glybera® for LPLD receives market authorization approval from the EMA, we will evaluate the most attractive method for commercializing this program, which may include establishing our own sales and marketing infrastructure, or may be done through a collaboration with a third party. The extent to which we are responsible for establishing or renting our own sales force and supporting infrastructure may have an impact on the level of future sales costs incurred by us.

#### Transaction opportunities

In line with our strategy to always consider transaction opportunities which may accelerate the path to sustainable and profitable growth or otherwise be beneficial to our business we are currently investigating, discussing and negotiating a number of opportunities that we believe may qualify as such.

### Significant accounting policies

For a summary of our significant accounting policies reference is made to note 2 (Summary of significant accounting policies) of the notes to the audited consolidated financial statements for the year 2009.

#### Critical accounting estimates and judgments

For a summary of our critical accounting estimates and judgments reference is made to note 4 (Critical accounting estimates and judgments) of the notes to the audited consolidated financial statements for the year 2009.

### **Treasury policies**

We do not have large receivables with external parties. The majority of our cash and cash equivalents are placed at Rabobank and ABN AMRO Bank.

Our costs and expenses are mainly denominated in Euro, as are our cash and cash equivalents. From time to time we may maintain limited deposits in other currencies such as US Dollars, Canadian Dollars and British Pounds as a hedge against costs and expenses

denominated in such currencies. The size of such deposits is never greater than the expected costs denominated in such currencies over the coming twelve months.

## No significant change

Except as set out in "Business – Outlook – Cash position", there has been no significant change in our trading or financial position since 30 June 2010, the date to which our most recent unaudited condensed consolidated interim financial statements were prepared.

## **Business**

#### Overview

We are a leader in the development of human gene based therapies. In December 2009, we filed a marketing authorization approval (MAA) with the European Medicines Agency (EMA) for Glybera®, our lead product, for Lipoprotein Lipase Deficiency (LPLD). We expect to be able to obtain an opinion from the EMA's Committee for Medicinal Products for Human Use (CHMP) on our filing in mid 2011 and if this opinion is positive, a decision from the European Commission for marketing authorization is expected to follow approximately two months thereafter. This puts us in a leading position in the field of gene therapy companies competing to bring a gene therapy product to commercialization. Our goal is to leverage our leadership position in this highly innovative field of gene therapy to build a specialty biopharmaceutical company for rare, mostly orphan diseases.

Gene therapy is a powerful new technique: by inserting therapeutic genes into human cells there is the promise of a cure of chronic, often hereditary diseases based on a single intervention. This may revolutionize the practice of medicine in inherited diseases, a field offering at present only limited treatment options. Gene therapy can also be applied to non-inherited diseases such as Parkinson's Disease where today there are only symptomatic treatment options.

Our pipeline consists of five programs. In addition to Glybera®, we have programs for Duchenne Muscular Dystrophy (AMT-080), Hemophilia B (AMT-060), Acute Intermittent Porphyria (AMT-021) and Parkinson's Disease (AMT-090).

Our lead product Glybera® is developed for the indication Lipoprotein Lipase Deficiency, a debilitating metabolic disorder. It has already demonstrated excellent results with clinically impressive effects in reducing the risk of pancreatitis while being well tolerated and generally safe. Pancreatitis is the most frequent, very painful and potentially life threatening clinical feature of LPLD. In December 2009 we submitted the MAA for Glybera® for LPLD to the EMA. We are now working towards an official response to the Day 120 questions raised by the CHMP, due by the end of 2010. Assuming no unforeseen adverse events or delays, we expect to receive the opinion of the CHMP on our filing mid 2011. If the CHMP's opinion is positive, a decision from the European Commission for marketing authorization is expected to follow approximately two months thereafter. We expect to be able to file for market approval in Canada in 2011 and in the United States by the end of 2011 or early in 2012. First sales of Glybera® for LPLD under a "named-patient-sales" program in France, are expected early 2011.

All of the programs in our pipeline are based on our Adeno Associated Virus (AAV)-based gene delivery technology platform and our baculovirus and insect cell based manufacturing platform. In focusing on AAV vectors, we are using gene delivery vehicles which are generally considered safe. We use different AAV vectors to target various organs or specific tissues, such as muscle or liver, and even to specific types of cells within these organs. By genetically engineering our AAV-based vectors with different therapeutic genes and tissue specific promoters we have a platform vector technology that is modular in approach, facilitating fast product design within short timelines.

We focus on developing innovative treatments for diseases with a significant unmet medical need. Our programs are either targeted at orphan diseases, or are driven by their potential to replace existing products that provide a sub-optimal level of care in substantial markets. For example, we aim to develop therapies which have the potential to improve existing, inferior

treatments, and also to substitute an entire market through providing a real cure as opposed to offering just symptomatic treatment.

Whilst there are more than 45 AAV-based gene therapy trials ongoing, there are only a few which are in Phase III clinical trials or in registration. One of our core strengths is that our staff has extensive experience of developing and registering specialty drugs.

We are located in Amsterdam, the Netherlands. We currently have 84 employees and have a staff of highly educated, skilled and experienced professionals. In addition, we have a world-class, 375 m², cGMP-licensed manufacturing facility. In this highly specialized facility we have manufactured batches for the clinical trials and here we can also produce the material for all the clinical trials for the products we are currently developing. The facility is fully validated for commercial production and has a capacity capable of producing enough material to supply our European and North American target markets with Glybera® for LPLD and for the next phases of development of the other programs currently in our pipeline.

### **History**

We were founded in 1998 by seven scientists who were investigating LPLD at the Academic Medical Centre of the University of Amsterdam (AMC), one of the largest academic hospitals in the world, and have since our inception been focused on the development of new technologies in gene therapy.

In our early years we were funded by the AMC, government grants, and from income derived from cGMP contract manufacturing of biologics for third parties. In July 2006, we raised €22 million in a private financing round with a group of venture capital investors. In June 2007, we completed our initial public offering and our shares were admitted to listing and trading on Euronext Amsterdam, raising an additional €56 million. In December 2009, we strengthened our financial position via a private placement of convertible bonds to funds associated with Forbion Capital Partners, raising €5 million.

In 2009, to control cash burn, in addition to our focus on getting Glybera® for LPLD on the market, we decided to focus our activities on the acceleration of four other programs in our pipeline - our programs for Duchenne Muscular Dystrophy, Hemophilia, Acute Intermittent Porphyria and Parkinson's Disease. Other projects were postponed or discontinued.

In January 2010, we were granted an innovation credit from the Dutch government for the development of our treatment for Duchenne Muscular Dystrophy.

In December 2009, we filed a marketing authorization application for Glybera® for LPLD for with the EMA.

#### Strategy

Our mission is to serve patients with serious chronic progressive, often inherited disorders, by providing a cure with a single treatment intervention. The goal is to become a specialty biopharmaceutical company which develops gene therapy products for diseases with a significant unmet medical need, and market these ourselves or via partnerships.

Our strategy to achieve this goal is based on three main elements:

Validate the gene therapy approach through the approval of Glybera®

Glybera® for LPLD is currently first in line for marketing authorization in Europe among all gene therapy products. If approved, this drug not only validates our capabilities and know how in bringing novel therapeutic cures to market, but also validates gene therapy in general as an innovative treatment approach.

Focus on innovative treatments for diseases with significant unmet medical need

We focus on building a specialty biopharmaceutical company delivering innovative treatments for diseases with a significant unmet medical need. Our programs are either targeted at orphan diseases, or are driven by their potential to replace existing products that provide sub-optimal solutions for substantial markets.

Orphan disease focus: Orphan diseases are rare (US: fewer than 200,000 people afflicted; EU: no more than five in 10,000 people afflicted) and usually life threatening or severely debilitating. More than 5,000 orphan diseases have been identified to date. 80% of these are believed to be caused by a single genetic defect. Orphan drugs are medicinal products specifically intended to treat orphan diseases. Various regulatory authorities have streamlined the approval process in order to better serve patients suffering from these diseases, thereby allowing orphan drugs to potentially get to market more quickly than drugs to treat non-orphan diseases. In addition, the regulatory frameworks in the US and EU and certain other jurisdictions encourage research into and development of orphan drugs by offering certain incentives such as market exclusivity-periods and fee waivers (for more information, see "Business - Government approval and product approval").

Of the programs in our pipeline, Glybera® and our programs for Acute Intermittent Porphyria and Duchenne Muscular Dystrophy are developed for orphan diseases and have attained "orphan designation". By focusing on orphan diseases we aim to secure a strong position in less competitive markets, whilst benefiting from relatively low development cost and relatively short development timelines and a relatively low cost sales infrastructure. Overall, we believe that there is significant profit potential in finding novel therapeutic solutions in areas of rare diseases where currently there is no approved therapy.

<u>Alternative therapies</u>: For many diseases treatments are only symptomatic, delivering a sub-optimal level of care. Despite this there are substantial, sometimes multi-billion dollar markets based on protein replacement, small molecules or antibodies treatments. Gene therapy could bring long time relief or even a cure for such conditions through a new treatment paradigm.

Our pipeline programs for Hemophilia B and Parkinson's Disease fall into this category, as they target large, yet sub-optimal care markets. Large pharmaceutical companies currently serving these markets have a significant interest in alternative therapies which may threaten their current business or provide opportunities to extend their stakes. Also, there may be interest from companies which wish to enter these markets. We believe that this may provide us with opportunities for early partnerships and early income.

### • "Build and partner" approach

We intend to be a company that develops products that we can commercialise ourselves as well as products which are more suited for commercialization via partnerships. We will aim to conclude such partnerships relatively early to generate revenues to provide non-dilutive funding. In general, we intend to commercialise products targeted at orphan diseases ourselves, whilst we believe that programs aimed to replace existing products could have much potential for lucrative early stage partnering.

Transaction opportunities, such as mergers and acquisitions, partnerships or collaborations, licensing transactions and acquisitions of additional pipeline products, technology or intellectual property, which may accelerate the path to sustainable and profitable growth or otherwise be beneficial to our business will always be considered in the normal course of our business.

### Gene therapy

For a number of diseases today there is no cure or therapy truly addressing the cause of the symptoms available. Existing therapies are mostly limited to symptomatic treatment. Millions of patients have to rely on constant medical care to help them manage their life-long progressive complaints, at significant cost and often without a chance of sustained success. Nearly 40 years ago, scientists began exploring the concept of curing diseases by providing "healthy" genes in diseases caused by damaged or faulty genes. This technique offers the potential for a long-term or even life-long cure.

Genes are the blueprint used by the body's cellular machinery to make the functionally active molecules ('proteins') in the cells of our body. This protein manufacture is called 'gene expression'. When for example the blueprint for making one of the blood clotting factor proteins is missing or mutated, then sufficient blood clotting will not happen at times when it is needed. The result is continued bleeding after (minor) trauma or surgery. Introducing a copy of the proper gene into the cell nucleus in principle restores the natural function of producing 'healthy' blood clotting factor, and bleeding can be prevented.

There are a number of diseases where there is more than one such blueprint involved. Gene therapy is still in its infancy, and today the majority of research focuses on diseases caused by only one erratic gene; this has applications for many of the hereditary diseases such as Duchenne Muscular Dystrophy. Such diseases (known as monogenic) are often less complex and better understood than diseases where more than one dysfunctional gene is involved in causing the illness. However, there are also opportunities to apply gene therapy in diseases caused by more complex pathology, as long as there is one particular protein playing a crucial role in the causation of the disease. Again, here it may be possible to halt or eradicate the disease with a gene therapy that promotes the natural function of that one relevant protein. Our program for Parkinson's Disease is an example of a therapy which has such aim.

In the past, gene therapy approaches could result in cancer or strong immune responses in patients. Long-term expression of genes in cells, needed to achieve long-term efficacy, was a problem and gene therapies could not be manufactured reliably. As a consequence, as far as we are aware to date only two gene therapy products have ever been approved for marketing, one solely in China and the other solely in the Philippines. In general, gene therapy is highly innovative and is now arriving in the last stage of the process of proving that it can be delivered safely and effectively. Currently, novel modes of therapeutic gene delivery show much promise, and doctors and scientists are working hard on further scientific breakthroughs.

### Key technologies and capabilities

We have developed a broad platform that we believe has helped to overcome major challenges which the gene therapy industry was facing. The following key technologies and capacities clearly differentiate our approach from other gene delivery systems:

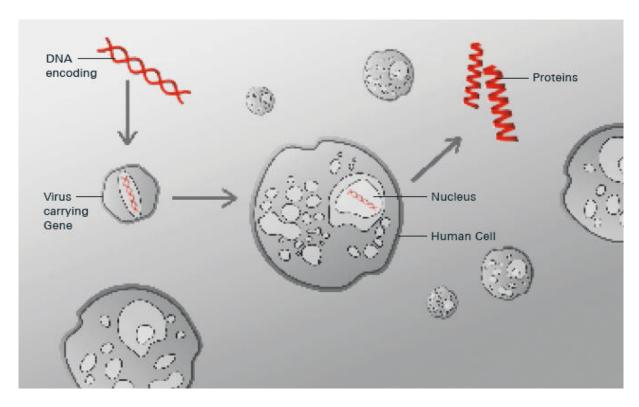
- Our platform vector technology
- Our platform manufacturing technology
- Our clinical development and regulatory expertise
- Our modular platform focused approach

### Platform vector technology

Our promising platform vector technology offers the potential for safe and effective gene delivery.

One of the key challenges in gene therapy is to identify a delivery vehicle, or 'vector', that can effectively and safely carry a gene into the target cells and into the nucleus. All our gene therapy products are based around Adeno Associated Virus (AAV) vector technology. AAV vectors are generally considered safe (Warrington and Herzog, Hum. Genet. 119 (2006); Tenenbaum, Lehtonen and Monahan, Current Gene Therapy 3 (2003); Monahan, Jooss, and Sands, Expert Opinion on Drug Safety Vol. 1, No. 1 (2002)) and have been tested in over 40 clinical trials to date (e.g. ClinicalTrials.org, J Gene Med, PubMed). 'Wild type', naturally occurring AAVs are non-pathogenic and do not in themselves cause disease in humans. We 'strip' the naturally occurring AAV before using it as a vector to carry the therapeutic genes, and through this we ensure that the vector used cannot replicate anymore. The genes in wild type and in our modified AAV vectors, in contrast to other viral gene delivery systems, do not integrate into the genome of the patient. Instead a stable 'extra-chromosomal' (i.e. nonintegrated) gene form is created in each nucleus, that also guarantees long-term, persistent activity in the target cells. Non-integration is an important factor in determining the safety of our vector technology as it essentially eliminates the risk of inducing cancer, a risk seen with some other, non-AAV vectors.

Efficacy in patients requires lasting therapeutic gene expression in the target tissue. The 'extra-chromosomal' form created after administration of the AAV-based gene therapy induces persistent therapeutic gene activity. Also, AAV can be used to target both dividing and non-dividing cells. Other gene therapy platforms cannot deliver genes into non-dividing cells. Targeting non-dividing cells or tissues has the added advantage of limiting loss of activity of gene therapy from loss of cells with good genes in them. Our experience with Glybera® for LPLD has demonstrated that our technology is able to provide multi-year tissue-targeted expression of the therapeutic protein after one-time administration.



### Platform manufacturing technology

Our platform manufacturing technology enables economically feasible and commercially scalable manufacturing.

In the past, the production of gene therapy products, especially AAV-based vectors, has been hampered by the challenges of scaling-up to commercial production (traditionally carried out in mammalian cells) in an economic way. To date this challenge still represents a major obstacle for almost all of our competitors. We have succeeded in developing a proprietary new platform manufacturing technology that allows safe, effective, cGMP compliant, economically feasible and commercially scalable manufacturing of our products. We consider this a major differentiating factor in gene therapy development.

Our novel approach is based on the use of a combination of baculoviruses and insect cells. It is a highly flexible process that can be easily and quickly adapted to produce a wide variety of products based on our vector technology, thereby significantly reducing the time needed for product development. We believe that our platform manufacturing technology enables full development and commercial-scale manufacturing of our lead product Glybera® for LPLD, and provides adequate capacity for the next phases of development of the other programs currently in our pipeline.

## Clinical development and regulatory expertise

Pharmaceutical companies have for long avoided the challenging field of gene therapy research. Gene therapies were regarded as too complex and risky. Gene therapy trials are therefore almost exclusively conducted by small, specialized companies and by academic groups. Major hurdles for those organizations are their clinical development and regulatory capabilities. These studies often (but not exclusively) focus on development of therapies for rare (ultra orphan) indications. One challenge for regulatory authorities with respect to orphan indications is the very low number of patients available for inclusion in clinical trials, the way studies have been carried out and consequently insufficient information on the safety and efficacy of individual products which makes it difficult to interpret the results.

We believe that we have all the necessary skills to advance a product through all stages of clinical development and to round off regulatory processes to filing. We have also established close links to the regulatory bodies and seek early discussions at all stages of development to ensure that our trials are in conformity with legal requirements. In developing and filing Glybera® for LPLD, we have managed the entire process without the support of a big partner. We believe that this capability has made us an attractive fit for a number of academic institutions with exciting early stage pre-clinical programs to enter into a collaboration with us, which may lead to opportunities to add new programs to our pipeline in the future.

### Modular platform focused approach

Using unique manufacturing technology we are able to package a wide range of therapeutic genes into the relevant vector in a modular way. Therefore, we expect to be able to address a large number of disease indications. Based on the modular concept of our technology - the same vector type may carry different genes for different diseases - there is the possibility of faster development times, lower cost of development and lower sales infrastructure.

### Programs and pipeline

The below table summarizes key information about our programs and pipeline.

Program	Organ	Discovery	Pre- clinical	Phase I/II	Phase II/III	Filed	Marketed	Orphan designation
Glybera® Europe	Muscle							EU/US
Glybera® US¹ & Canada¹	Muscle							EU/US
Glybera® HLP52	Muscle							EU/US
Duchenne Muscular Dystrophy	Muscle							EU/US
Hemophilia B	Liver							-/-
Acute Intermittent Porphyria	Liver							EU/-
Parkinson's Disease	Brain							NA

- 1 US: Currently awaiting finalization of pre-BLA discussion with the FDA; Canada: Pre-NDS meeting held with Health Canada.
- Phase I complete; Phase II proof of concept required. Further development to be carried out under a partnership with a third party (see also "Business Glybera® for Lipoprotein Lipase Deficiency Glybera® for other Hyperlipoproteinemia)

#### Glybera® for Lipoprotein Lipase Deficiency

Disease background of Lipoprotein Lipase Deficiency

Lipoprotein Lipase Deficiency (LPLD) is a seriously debilitating disease caused by mutations in the Lipoprotein Lipase (LPL) gene, resulting in highly diminished or absent activity of the LPL protein in patients. This protein is needed in order to break down large fat-carrying particles that circulate in the blood after each meal. When such particles, called chylomicrons, accumulate in the blood, they may obstruct small blood vessels. The clinical result is recurrent acute inflammation of the pancreas, called pancreatitis. Mortality of severe pancreatitis attacks is around 15%, based on the mortality in the control arm of a very recent intervention study in acute pancreatitis published in The Lancet. The disease can also result

in difficult-to-treat diabetes, an increased risk of cardiovascular complications, and is associated with significant morbidity and mortality. There is currently no treatment or cure for LPLD available. Clinicians advise LPLD patients to adhere to a stringent diet allowing virtually no fat, but this does not entirely prevent the occurrence of pancreatitis and the other disease related complications.

Most patients suffering from LPLD are undiagnosed, which makes it difficult to accurately establish disease prevalence. The literature offers no consistent estimate of LPLD prevalence, with some reports indicating approximately one patient per million of population. In our estimate of LPLD prevalence, we rely on the research conducted by Dr. John Kastelein and Dr. Michael Hayden, both medical authorities in the field of LPLD. Based on their research, we estimate LPLD prevalence to be approximately two patients per one million individuals (see also Gaudet, De Wal, Tremblay, Déry, Van Deventer, Freidig, Brisson and Méthot, Atherosclerosis Supplements, Volume 11, Issue 1 (2010)). The prevalence is significantly higher in certain areas such as in the province of Quebec, Canada, where a strong founder effect exists. We estimate overall LPLD prevalence in the European (European Union and Turkey) and North American (United States and Canada) markets to be approximately 1,600 patients in total.

Glybera® is a gene therapy, which restores the LPL enzyme activity required to process the fat carrying particles after meals. Glybera® has shown clear evidence that it reduces the frequency of pancreatitis. Glybera® therapy is administered once only, such single administration expected to be effective for many years and possibly for life. While it may represent a challenge in terms of reimbursement, this simple dosing regimen is of great advantage to the patient.

Considering the severity of LPLD and the lack of any alternative therapy, we expect that, if market approval is obtained, Glybera® will reach high market penetration. The time course of market penetration is likely to be affected by the rarity of the disease impacting difficulties in patient identification and diagnosis. Focused educational initiatives and the availability of an easy to use companion diagnostic - such as the LPLchip, a diagnostic tool to rapidly diagnose patients with LPLD that we are developing together with Progenika Biopharma - are expected to improve this. We anticipate that the majority of the identified LPLD patients in Europe and North America would eventually be treated with Glybera® if market approval is obtained, which would be in line with the situation for other approved orphan drugs.

### Stage of development

We filed Glybera® for LPLD for marketing authorization with the EMA on 23 December 2009 and the EMA commenced its formal review on 20 January 2010. The data package accompanying our submission of Glybera® includes three clinical studies conducted in the Netherlands and in Canada, in which a total of 27 LPLD patients were administered the drug. Follow-up studies are ongoing.

In all trials we conducted, the therapy proved to be well tolerated and safe. Importantly, a single administration of Glybera® resulted in a long-term clinically important reduction in the occurrence of acute pancreatitis episodes. The frequency of new pancreatitis episodes – which represent the most debilitating complication of LPLD - was reduced.

We have had two meetings with the Committee for Advanced Therapy (CAT) at the EMA for clarification about the Day 120 questions (see "Business - Government approval and product approval"). These meetings have enabled us to finalize our strategy for responding to these questions in a timely and effective manner. The outcome of the meetings suggests that we will not be required to conduct more clinical trials with additional new patients to be treated at this time; the responses to the Day-120 questions will be based in part on additional data and

analyses from patients treated with Glybera® in clinical trials for which long term follow up is ongoing, which will supplement the data package previously provided. We are now working towards an official response to the Day 120 questions, due by the end of 2010. We are going to provide an overview to what extent further data will become available in the official Day 120 response, following which the CAT has the opportunity to ask for further data in the second round of questions at Day 180. This will include new data available from the last clinical trial (CT-AMT-011-02 EXT). We expect that if we are granted marketing authorization, the authorization granted to us shall be a "marketing authorization based on exceptional circumstances" (see "Government regulation and product approval – General regulation in the European Union – Marketing approval").

Glybera® for LPLD has received orphan drug designation from the regulatory authorities in Europe and the United States. Due to the nature of the underlying disease and its low prevalence we do not expect that a competitive treatment will be developed which could prevent us from getting orphan drug status.

### Expected next milestone

We are now working towards an official response to the Day 120 questions, due by the end of 2010. Assuming no unforeseen adverse events or delays, we expect to receive the opinion of the CHMP on our MAA mid 2011. If the CHMP's opinion is positive, a decision from the European Commission for marketing authorization is expected to follow approximately two months thereafter.

In various jurisdictions it is possible to allow patients in critical disease stages early access to innovative therapies which are still under regulatory review on the basis of a nationally approved "named-patient sales program". Assisted by a specialized consulting and sales company we have taken steps to implement a named-patient sales program in France, to make the product available to LPLD patients in need. Currently, we are collaborating with a panel of experts who are reviewing the available data against the patient population they care for, so they may propose early access to the French regulatory authority (*Agence Française de Sécurité Sanitaire des Produits de Santé* – AFSSAPS). We expect the first 'early access' patient in France will be dosed early in 2011, prior to the CHMP opinion on our MAA and the decision from the European Commission for marketing authorization.

We intend to also seek permission to market Glybera® in Canada and, later, in the US. Filing in Canada is anticipated for 2011. We expect to receive either special protocol advice in preparation for an investigational new drug (IND) application in the US in the course of 2011 or file a biological license application (BLA) for approval in the United States at the end of 2011 or early 2012. The eventual path forward in Canada and the United States will depend to a large extent on the opinion of the EMA.

### Commercialization strategy

We are currently evaluating the most efficient route for bringing Glybera® for LPLD to individual geographic markets if and when market approval is obtained. The options include building our own commercial and support organization or engaging in commercial partnerships, or a combination thereof. Decisions on this are driven by the structures and dynamics of the various healthcare markets, the availability of potential partners that already have sales forces active in the target segments suitable to exploit potential synergies and accelerate the commercialization of Glybera® for LPLD, and cost efficiencies.

### Glybera® for other Hyperlipoproteinemia

After completion of the development of Glybera® for LPLD, Glybera® may potentially be developed patients suffering from а more widespread condition 'Hyperlipoproteinemia type 5' (HLP5). HLP5 patients exhibit a more modest inability to metabolize dietary fats than LPLD patients, yet also may have an elevated incidence of pancreatitis, diabetes, early atherosclerosis and other debilitating conditions and are likely to benefit significantly from Glybera® if the root cause of their condition is related to LPL mutations. Additional clinical trials will be required to develop Glybera® for this expanded patient population. Based on our own research, we currently estimate the target HLP5 patient population in the European and North American markets at approximately 70,000 in total. However, additional genetic studies and diagnostic data - which may for instance be generated by the LPLchip we are currently developing with Progenika Biopharma - are needed to verify this estimate. Glybera market expansion clinical trials for HLP5 will most likely only be started if a partner for Glybera for HLP5 is interested in funding them.

### AMT-080 for Duchenne Muscular Dystrophy

### Disease background of Duchenne Muscular Dystrophy

Duchenne Muscular Dystrophy (DMD) is a particularly severe and progressive disease that shows itself early in young children, almost exclusively boys. The disease is caused by mutations in the dystrophin gene, which is located on the X-chromosome, which prevent the production of functional dystrophin protein. As dystrophin plays a critical role in muscle maintenance, the disease causes progressive weakening of all muscles. Most patients die when the heart or those muscles that control breathing no longer function adequately. Currently there is no cure available; patients die in young adulthood. Innovative gene therapy approaches provide the big promise of preventing this fatal disease outcome with a single treatment.

We are developing a gene therapy product, research code name AMT-080, based on 'exon skipping' technology which aims to effectively bypasses (skipping) the gene mutation so that functional dystrophin protein can be produced.

We have demonstrated, in a mouse model of the disease, lifetime therapeutic efficacy of a single treatment. More recently, we have shown successful delivery of this therapy in the heart and skeletal muscles of mice. We are further developing the delivery methodology and optimizing the technique for delivery to skeletal muscles using a porcine model. These latest results are expected to be a good predictor for the efficacy of this approach in humans and therefore represent an important value inflection point in the development of this program.

#### Stage of development

Preclinical studies were performed in collaboration with Professor Irene Bozzoni's group at the University of Rome.

In January 2010, we were granted an innovation credit from the Dutch government for the development of our treatment for Duchenne Muscular Dystrophy (see also "Operating and Financial Review –Contractual obligations").

We have orphan drug designation in Europe and the United States on this program.

### Expected next milestone

We are currently evaluating whether development of a product for the heart and breathing muscles with a goal to prevent death of patients would be complementary to other approaches focusing on skeletal muscles and would provide a faster and effective route to market. Alternatively we may consider developing a product for the whole body, although this would likely increase development times and risk.

Clinical trials are expected to start in 2012.

### AMT-060 for Hemophilia B

### Disease background of Hemophilia B

Hemophilia B is a serious inherited orphan disease characterized by repeated and sometimes life threatening episodes of external and internal bleeding after accidental trauma or medical interventions. The episodes may cause long-term damage, for instance to the joints, and may be fatal if they occur in the brain. The defect in blood clotting in Hemophilia B is caused by the lack of functional clotting of the factor IX protein as a result of mutations in the gene encoding this protein. Protein replacement is the current standard of care. Frequent intravenous administrations of recombinant factor IX are required to stop or prevent bleeding. Protein replacement therapy is costly (US\$ 150,00 - 200,000 per patient per annum), cumbersome, and does not completely prevent bleeding.

Administered once, our Hemophilia B gene therapy, research code name AMT-060, aims to restore the function of blood clotting long-term through the introduction of the functional gene for the factor IX protein into the patients' liver cells.

### Stage of development

Our collaboration partners with St Jude Children's Research Hospital in Memphis, Tennessee and the University College of London have started a Phase I/II explanatory clinical trial to assess the safety and efficacy of different doses of Hemophilia B in a dose escalation gene therapy study. We will build on the outcome of this trial, and are preparing for additional clinical development work to establish safety, tolerability and proof-of-concept with a factor IX gene therapy using our proprietary, clinically validated production system. In addition, we are exploring ways of expanding our Hemophilia program to also include Hemophilia A, the same disease with a significantly higher incidence.

## Expected next milestone

In the next months further patients will be dosed in this study and results will be available in 2011. We expect further clinical studies to begin in 2012.

### Commercialization strategy

Protein replacement therapy for Hemophilia B has a large market of approximately US\$ 1.5 billion (*EvalueServe market research*). We believe that our Hemophilia B program has partnering potential as it has the potential to substitute protein replacement therapy if market approval is obtained. We currently intend to partner the product.

### AMT-021 for Acute Intermittent Porphyria

### Disease background of Acute Intermittent Porphyria

Acute Intermittent Porphyria (AIP) is a rare liver metabolic disorder resulting from mutations in the PBDG gene which encodes for the enzyme porphobilinogen deaminase, a liver protein necessary for the production of heme. Insufficient activity of this protein leads to an accumulation of toxic metabolites resulting in a wide variety of problems, including acute, severe abdominal pain, muscular weakness and an array of neurologic manifestations, including psychiatric episodes, seizures and coma. In the majority of cases, attacks are triggered by precipitating factors such as hormonal fluctuations, infections, drugs and dietary changes. Long-term consequences may include irreversible nerve damage, liver cancer and kidney failure. Acute porphyric attacks can be life-threatening and currently available therapies do not prevent them nor do they prevent their full consequences.

Our program for AIP, research codename AMT-021, is intended to provide long-term normalization of the PBGD protein in order to prevent acute attacks and their complications.

## Stage of development

We have demonstrated that our program results in normalization of the PBGD protein in an animal model of AIP. It completely prevented the occurrence of attacks and significantly ameliorated the neuropathy that develops in untreated mice. Our partner Center for Applied Medical Research (*Centro de Investigación Médica Aplicada -* CIMA), a research consortium founded by the University of Navarra, Spain, has shown expression of genes in the liver for more than a year, using AAV-mediated delivery methods similar to AMT-021's AAV-based delivery system.

We have orphan drug designation in Europe on this program.

### Expected next milestone

Preclinical toxicology testing is anticipated to start in 2011, and we anticipate that our partner CIMA – also an expert center for treating AIP patients – will begin enrolling patients for a clinical trial in 2012.

#### Commercialization strategy

We currently intend to commercialize the product ourselves, if market approval is obtained.

#### AMT-090 for Parkinson's Disease

### Disease background of Parkinson's Disease

Parkinson's Disease (PD) is a neurodegenerative disorder that affects the sufferer's motor skills, speech, and other functions so that every action becomes increasingly difficult and eventually impossible. The symptoms are caused by degeneration and death of nerve cells in the part of the brain that produces dopamine - a chemical which sends messages in the brain to control movement - and other neuro-transmitters. At present, there is no cure for Parkinson's Disease, but medications or surgery can provide relief from the symptoms. The most widely used form of treatment is L-dopa in various forms, which is converted to dopamine in the central nervous system. From previous studies – preclinical and clinical - there is a consistent line of evidence that the infusion of GDNF protein into the brain is

effective in Parkinson's Disease. GDNF (glial cell-derived neurotrophic factor) stimulates the formation of dopamine and prevents further degeneration of dopaminergic neurons.

### Stage of development

We have started preclinical research of a gene therapy, research code name AMT-090, that will introduce the gene coding for the GDNF protein to provide a consistent supply of GDNF to the relevant areas of the brain. We are conducting initial research with the University of Lund, Sweden.

### Expected next milestone

We have recently finalized pre-clinical tests in rodents and expect to establish proof of concept in rats by the end of 2010. We also started pre-clinical testing in non-human primates and aim to establish proof of concept in 2011. We plan to start clinical development in 2012.

## Commercialization strategy

Parkinson's Disease is a multi-billion dollar market with symptomatic treatment only, the efficacy of which declines over time and which creates significant side effects and comorbidities (such as depression, etc.). We are looking at funding or partnering the project in the short- to mid-term by way of finding a collaboration partner.

### Competition

We believe that our AAV-based platform puts us in a strong position relative to competitors in gene therapy, for instance compared to the competition using lentiviral technology or AAV-based technology based on a traditional mammalian production platform. Based on our technology the lentiviral technology not only has an unfavourable carcinogenicity profile but also faces scalability issues, which will likely result in high cost of goods. The traditional mammalian production platform generally faces production scalability issues.

There have been prominent failures of gene therapy companies in the past – even when AAV-based. We believe that gene therapy companies can now be more successful than they were in the past. Both choice and development of vectors, as well as optimization of vectorgene constructs, have evolved significantly over recent years. For example, previously the use of AAV 2 vectors in Hemophilia has shown low expression levels and significant immune reactions. Today, optimized constructs based on other vector serotypes (we currently use AAV 1, 5 or 6) have shown higher expression levels requiring lower viral concentrations.

Several companies operate in the related but distinct area of gene therapy-based cancer immunotherapeutics. These companies, however, do not compete with us, as we currently do not develop medicines for cancer. The gene therapy technology applicable to cancer treatment is very different from that employed by us.

## Research and development strategy

Our internal investment in research is focused on developing innovative treatments for diseases with a significant unmet medical need and furthermore targeted at highly promising technology areas expanding the value of our technology platform. In line with this strategy we are currently developing technologies of using vectors to deliver small interfering RNA (siRNA) to the cell nucleus to silence genes. siRNA products have often failed because of their inability to reach their targeted cell. Adeno-associated vectors allow efficient, safe, long-term gene delivery in a wide range of tissues and therefore are excellent vectors to deliver

silencing molecules as it can inhibit the production of a disease-related mRNA by RNA interference (RNAi). We have successfully silenced a gene (ApoB100) in mice showing a long lasting effect on cholesterol lowering. To contain cost we intend to partner this promising research project.

## Intellectual property

#### Introduction

We consider patents and other intellectual property rights to be vital to the success of our business. We are continuously working to improve the protection of our technology as well as identifying and obtaining access to know-how for our pipeline products from third parties. As such, our intellectual property portfolio is continuously developing.

We have filed certain patent applications for our proprietary baculovirus production technology and in relation to our specific product pipeline. In addition, patents covering certain gene variants and treatment applications have been assigned to us by the AMC. Furthermore, we in-license rights from third parties related to the AAV vector production technology and certain genes and promoters. While some patents or licenses apply to several of our products, we may also need to apply for patent protection for or obtain a license from a third party in respect of product specific components.

## Intellectual property strategy

It is our policy to actively seek patent protection for our inventions and technologies and their uses. We analyze the results of our research and development activities regularly to identify patentable subject matter and file new patent applications. In our dealings with our main collaborators we always ensure that we have rights in the intellectual property that results.

The Board of Management and our Senior Management have considerable individual and collective experience in the acquisition and management of intellectual property rights.

Whilst patents are the cornerstone of our proprietary protection, whether owned by us or inlicensed, in addition we make use of trade secrets. 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. Glybera® is a registered trade mark in various jurisdictions including the EU. We will, in due course, make appropriate trade mark filings for our various other products.

We are reviewing the IP landscape for each of our products as part of the decision making process as to whether or not to continue development. If we identify third party patents that are reasonably likely to be valid and enforceable at that point, which may dominate our planned activities, we shall seek licenses at that time.

Our business is in a complex technical area due to the nature of the design of the products and their process of production and in this field there are many patents and patent applications, both published and unpublished. We only seek licenses to issued claims of third party patents where it is necessary to do so because the claims of such patents are reasonably likely to be valid and enforceable. We actively monitor the third party patent applications of which we are aware, but it is our policy not to seek licenses prior to any applicable patent application proceeding to grant when the granted claims become clear. When any of our products is in clinical development we review the intellectual property landscape for freedom to operate issues on an ongoing basis. If we identify third party

patents that may cover our activities, which does occur from time to time in our field, we then conduct detailed validity analysis of any identified patents because the patent rights in question may be invalid and if so we would not approach the third party and seek a license to such rights. Where we conclude relevant patents are weak and in jurisdictions where it is possible to oppose the validity of such patents, it is our policy to do so. If we conclude that the patent is likely valid we then determine a potential licensing strategy and approach the third party in question.

### Intellectual property portfolio

Our intellectual property portfolio contains (solely owned, jointly owned and in-licensed) patents, trademarks and other intellectual property rights. For an overview of our intellectual property portfolio we refer to the report of Haseltine Lake LLP, European Patent and Trade Mark Attorneys, included in this Prospectus as Annex 1.

Our patent portfolio consists of solely owned, jointly owned and in-licensed patents. The in-licensed patents that we deem material to Glybera® for LPLD are in-licensed on the basis of the below license agreements.

- We have entered into an exclusive worldwide commercial license agreement with Xenon Genetics Inc. on 18 June 2001, under which we have obtained worldwide rights to use, manufacture and commercialize intellectual property covering certain LPL genes in the field of gene therapy to treat LPL deficiency and coronary artery disease. This agreement required us to pay an upfront signature fee and requires us to pay both milestones and royalties to the licensor.
- We have entered into an exclusive worldwide commercial license agreement with a
  major pharmaceutical company on 13 November 2006, under which we have
  obtained rights in the major markets to use, develop, manufacture and commercialize
  intellectual property covering a LPL gene in the field of gene therapy to treat LPL
  deficiency. This agreement required us to pay an upfront signature fee and requires
  us to pay both milestones and royalties to the licensor.
- We have entered into a non-exclusive worldwide commercial sublicense agreement with Targeted Genetics Corporation on 5 December 2006, under which we have obtained worldwide rights to commercialize the AAV1 capsid serotype used in Glybera® for LPLD. The license agreement required us to pay an upfront signature fee and requires us to pay both milestones and royalties to Targeted Genetics Corporation.
- We have entered into a non-exclusive worldwide commercial license agreement with Protein Sciences Corporation on 22 March 2007 in relation to the use of Spodoptera Frugiperda cells in relation to the AAV vector used in the manufacture of Glybera® for LPLD. The license agreement required us to pay an upfront signature fee and requires us to pay an annuity.
- We have entered into a non-exclusive worldwide commercial license agreement with the National Institutes of Health on 2 May 2007 to produce AAV in insect cells. The license agreement required us to pay an upfront signature fee and requires us to pay both milestones and royalties to the licensor.
- We have entered into a non-exclusive worldwide commercial license agreement with leading research institution Salk Institute for Biological Studies on 8 February 2008, under which we have obtained rights to commercialize technology that is a

component for Glybera for LPLD. The license agreement required us to pay an upfront signature fee, and requires us to pay both an annual license maintenance fee and royalties to the licensor.

 We have entered into a non-exclusive worldwide commercial sub-license agreement with a biopharmaceutical company on 3 September 2010 in relation to the intramuscular administration of Glybera® for LPLD. The license agreement required us to pay an upfront signature fee and requires us to pay an annuity.

### Strategic partnerships

We have entered into a number of strategic partnerships with academic centers concerning the research and development of our programs. The most important of such partnerships are summarized below.

### Center for Applied Medical Research

We are collaborating with the Center for Applied Medical Research (Centro de Investigación Médica Aplicada - CIMA), a research consortium founded by the University of Navarra, Spain, and certain related parties in developing our program for Acute Intermittent Porphyria. Under the terms of the collaboration we have been granted a worldwide exclusive right to commercialize the final product we are jointly developing. CIMA is entitled to certain milestone and royalty payments. Together with CIMA and certain other parties we have formed a consortium that is applying for EU funding (under the Seventh Framework Programme for research and technological development (FP7)) of the pre-clinical and clinical trials that CIMA will conduct up to completion of the Phase I/II studies.

### St Jude Children's Research Hospital

We are collaborating with St Jude Children's Research Hospital in Memphis, Tennessee in developing our program for Hemophilia B. Under the terms of the collaboration, we have amongst others been granted a worldwide exclusive right to commercialize the final product we are jointly developing. St Jude Children's Research Hospital is entitled to certain milestone and royalty payments. As part of the collaboration we also sponsor research into Hemophilia B at and by St Jude's Children's Research Hospital.

### Government regulation and product approval

Our business is subject to extensive government regulation. Regulation by governmental authorities in the United States, the European Union, Canada and other jurisdictions is a significant factor in the development, manufacture and marketing of any drugs and in ongoing research and development activities. All of our products will require regulatory approval by governmental agencies prior to commercialization including rigorous pre-clinical trials and other pre-marketing approval requirements by the FDA, the EMA and other regulatory authorities in the US, EU and in other jurisdictions.

### Orphan drug regulation

The regulatory framework in the US and in the EU encourages research into and development of orphan drugs. The primary incentive in the EU is a ten-year period of market exclusivity along with compassionate use (allowing certain patients access to drugs before regulatory approval is granted, under certain circumstances), fast track approval, reduced fees and research grants.

Regulation 141/2000 states that a drug shall be designated as an orphan drug if its sponsor can establish (a) that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the Community when the application is made or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the Community and that without incentives it is unlikely that the marketing of the drug in the Community would generate sufficient return to justify the necessary investment and (b) that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the Community or, if such method exists, the drug will be of significant benefit to those affected by that condition. Regulation 847/2000 holds criteria for the designation of orphan drugs.

Similar legislation exists in the US. In the US, a rare disease or condition is statutorily defined as one affecting less than 200,000 individuals in the US, or one that affects more than 200,000 individuals in the US and for which there is no reasonable expectation that the cost of developing and making available the drug for the disease or condition will be recovered from sales of the drug in the US. Orphan drug designation may qualify a company for incentives under the Orphan Drug Act 1982 such as tax credits, fee waivers for regulatory submissions and marketing exclusivity for seven years following the date of the drug's marketing approval by the FDA. The FDA's Office of Orphan Products Development coordinates with the responsible drug evaluation centre to provide clinical study design assistance.

If a drug that has orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the approved drug will obtain the orphan drug status and is entitled to marketing exclusivity (ten years in the EU and seven years in the US). More than one sponsor may receive orphan drug designation for the same product (but only if they can demonstrate clinical superiority of the subsequent product) but only one sponsor will receive orphan drug status for the same product for the same rare disease or condition. The period of exclusivity begins on the date that the marketing authorization application is approved by the regulatory authority and applies only to the indication for which the product has been designated. In the US the FDA could approve a second application for the same drug for a different use or a second application for a clinically superior version of the drug for the same use.

## General regulation in the United States

The testing, manufacturing, labeling, advertising, promotion, distribution, export and marketing of our products are subject to extensive regulation by governmental authorities in the US. The FDA, under the Federal Food, Drug and Cosmetic Act, regulates the approval and marketing of pharmaceutical drugs in the US. Our products would be classified as biologics. The testing and approval process requires substantial time, effort and financial resources, and the receipt, timing, and conditions of any approval are uncertain and include, amongst others:

- pre-clinical laboratory models and tests, including animal testing;
- the submission to the FDA of an investigational new drug application (IND) for human clinical testing,
- which must become effective before human clinical trials commence;
- adequate and well controlled human clinical trials to establish the safety and efficacy of the drug;

- the submission to the FDA of a biologic license application (BLA); and
- assess compliance with current cGMP and, at the FDA's option, an FDA audit of the clinical trial sites that.

Pre-clinical studies include laboratory evaluations of the products, model studies to assess the potential safety and efficacy of the product, and testing in animals.

#### Clinical trials

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

Phase I clinical trials are usually conducted with a small number of healthy individuals to determine the metabolic and pharmacological activities of the product, to test its safety and, if possible, to obtain early evidence of efficacy. Phase II clinical trials usually involve studies in a limited patient population to determine the efficacy of the product for specific indications and to determine dosage tolerances and optimal dosage. Phase III clinical trials usually are conducted to evaluate clinical efficacy and to test safety within an expanded patient population.

Clinical trials typically are conducted in three sequential phases prior to approval, but the phases may overlap.

### Marketing approval

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

The FDA has 60 days from its receipt of a BLA to accept it for filing. Once accepted for filing, the FDA begins an in-depth review. Most applications for non-priority drug products are reviewed within ten months. The review process may be extended by FDA for three additional months to consider certain information or clarification regarding information already provided in the submission.

Before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with current good manufacturing practices is satisfactory and the BLA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

As a condition of BLA approval, the FDA may require substantial post approval testing and surveillance to monitor the product's safety or efficacy and may impose other conditions, including labeling restrictions which can materially affect the potential market and profitability of the product. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Further, the FDA closely regulates the post-approval marketing and promotion of drug and biologic drugs, including standards and regulations for direct consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. In addition, the FDA has broad post-market regulatory and enforcement powers, including the ability to suspend or delay issuance of approvals, seize or recall products, withdraw approvals, enjoin violations and institute criminal prosecution. The cost of preparing and submitting a BLA is substantial.

### Pharmaceutical pricing and reimbursement

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

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business.

### General regulation in the European Union

Clinical trials, the regulatory approval process, and safety monitoring of medicinal products and their manufacturers in the European Union proceed in much the same manner as they do in the United States. Therefore, many of the items discussed above under "General regulation in the United States" apply similarly in the context of the European Union. In addition, drugs are subject to extensive price and reimbursement regulation of the European Union member states.

### Clinical trial approval

Pursuant to the Clinical Trials Directive 200l/20/EC, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, approval must be obtained from the competent national authority of a European Union member state in which it is the plan to conduct the study. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application which must be supported by an investigational medicinal product dossier with supporting information prescribed by the Clinical Trials Directive and further detailed in applicable guidance documents. Manufacturing of investigational products is subject to the holding of authorization.

#### Marketing approval

Drugs defined as medicinal products developed by means of biotechnological processes must undergo the centralized approval procedure for marketing authorization, which, if granted, is automatically valid in all European Union member states and certain EEA countries. For advanced medicinal therapy products (ATMPs), including gene therapy

products, the centralized procedure is mandatory as well. The EMA and the European Commission administer the centralized marketing approval process.

In the marketing authorization application (MAA) the applicant has to show that the medicinal product concerned shows a significant positive outcome of a benefit-to-risk analysis and that therefore the granting of an authorization is in the interest of patients at a Community level. Under the centralized approval procedure, the EMA's Committee for Medicinal Products for Human Use (CHMP) serves as the scientific committee that renders opinions about the safety, efficacy and quality of human products on behalf of the EMA. For ATMPs the Committee for Advanced Therapies (CAT) was recently formed to support the CHMP. If the CHMP concludes that safety, efficacy and quality of the product is sufficiently proven, it adopts a positive opinion. This is sent to the European Commission to be transformed into a marketing authorization valid for the whole of the European Union. The CHMP has 210 days to give its opinion to the European Commission as to whether a marketing authorization should be granted. In the course of the 210 day-period there are 'clock stop periods' for answering questions raised by the CHMP, e.g. at 'Day 120'.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate in the application that he is unable to provide comprehensive data on efficacy and safety under normal conditions of use, because either the indications for which the product is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of the scientific knowledge, comprehensive information cannot be provided or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, the marketing authorization under exceptional circumstances is granted subject to the requirement for the applicant to introduce specific risk management procedures, in particular concerning the safety of the medicinal product, notification to the competent authorities of any incident relating to its use and action to be taken. The marketing authorization under exceptional circumstances is reviewed annually to reassess the risk-benefit balance in an annual re-assessment procedure.

### Manufacturing and manufacturers' license

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

#### Reimbursement

In the EU, the pricing and reimbursement mechanisms by private and public health insurers vary by country. In respect of the public systems reimbursement for standard drugs is determined by guidelines established by the legislator or responsible national authority; special rules may apply to orphan drugs. Inclusion of orphan drugs in reimbursement systems focuses on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any drug. Additionally the fulfillment of the medical need of individuals suffering from rare diseases is accepted to be a societal 'obligation' if overall budget impact is limited and if the marketing companies are acknowledged to have gone to

great ends to make the orphan drugs available. Acceptance for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. For expensive drugs in addition results based rules of reimbursement may apply.

### General regulation in Canada

Drugs sold in Canada are regulated by the Canadian Food and Drugs Act and the regulations made under that act. Even though a drug, medical product or device may be approved for use in another jurisdiction, it may not be sold in Canada until approved by Health Canada.

### Clinical trial approval

The Canadian Food and Drugs Act and underlying regulations require licensing of manufacturing facilities, carefully controlled research and testing of products, governmental review and approval of test results prior to marketing of therapeutic products, and adherence to cGMP and principles of Good Clinical Practices, as defined by each licensing jurisdiction, during production. The principal activities which must be completed prior to obtaining approval for marketing of a therapeutic drug product are essentially the same in Canada as in most major markets of the world and comprising of the performance of pre clinical animal studies and the Phase I, II and III clinical studies. A clinical trial application (CTA) must be filed by the company sponsoring the drug and accepted by either the Therapeutic Products Directorate (TPD) or the Biologics and Genetic Therapies Directorate (BGTD) of Health Canada before each of Phases I to III of human clinical trials may begin. The CTA application must contain specified information including the results of the pre-clinical or clinical tests completed at the time of the CTA application. In addition, since the method of manufacture may affect the efficacy and safety of a drug, information on chemistry and manufacturing methods must be presented. Health Canada conducts inspections to determine compliance with cGMP. Good manufacturing practices and quality control procedures must be in place.

The sponsor is required to conduct critical analyses of the adverse drug reactions annually or whenever requested to do so by the Director, and to provide a report. The sponsor is also required to inform Health Canada of, among other things, any changes to previously authorized CTA, and any updates made to the investigator's brochure.

### Marketing approval

Upon completion of all clinical studies, the results are submitted to the TPD or BGTD as part of a new drug submission (NDS). If, at the completion of a new drug review, it is concluded that the benefits outweigh the risks and that the risks can be mitigated and/or managed, the product is issued a letter known as a notice of compliance (NOC) which permits marketing of the product in Canada. The review process typically takes between 12 and 24 months from the date a NDS is submitted.

In addition, any product that is manufactured or distributed pursuant to Health Canada approval is subject to extensive continuing regulation by Health Canada, including record-keeping and labeling requirements and reporting of adverse events with the product. If any modifications to a product are proposed, including changes in the manufacturing process, manufacturing facility or labeling, a supplement to the NDS is required to be submitted to Health Canada.

Health Canada conducts post-market surveillance programs to monitor a product's side effects. Results of post-marketing programs may limit or expand the further marketing of products. A serious safety or efficacy problem involving an approved drug or medical device may result in Health Canada action requiring withdrawal of the product from the market.

#### Price review

The Patented Medicine Prices Review Board (PMPRB) is an independent quasi-judicial administrative agency created in 1987 under the Canadian Patent Act. Its mandate is two-fold:

- Regulatory: to ensure that the manufacturers' (ex-factory) prices of patented medicines sold in Canada are not excessive. The PMPRB reviews the price at which a drug product is sold by the manufacturer to all purchasers, including wholesalers, pharmacies, hospitals and others.
- Reporting: reports annually to Parliament through the Minister of Health on drug price trends of all medicines; on cost drivers and drug utilization for public drug plans; and on the research and development performance of pharmaceutical patent-holding manufacturers.

The PMPRB is responsible for regulating the price charged by patentees for prescription and non-prescription patented drugs sold in Canada to wholesalers, hospitals or pharmacies for human and veterinary use to ensure that they are not excessive.

Patentees are required to comply with the Patent Act to ensure that prices of patented medicines sold in Canada are not excessive. In the event that the PMPRB finds, after a public hearing, that a price is excessive in any market, it may order the patentee to reduce the price and take measures to offset excess revenues it may have received.

## Provincial and territorial government

The provincial and territorial governments are responsible, among other things, for providing public drug benefit plans to certain segments of their population (all provinces and territories provide coverage to seniors and those receiving social assistance) and managing the list of drugs for which public reimbursement from government drug plan is available. In some cases, drugs have a restricted status limiting coverage to particular types of patients or situations.

### **Facilities**

Our offices and laboratory space are located at Meibergdreef in Amsterdam, the Netherlands. Our Amsterdam location also houses our world-class, 375 m², cGMP-licensed manufacturing facility. In this highly specialized facility we have manufactured batches for the clinical trials and here we can also produce the material for the clinical trials for the products we are currently developing. The facility is fully validated for commercial production and has a capacity capable of producing enough material to supply our European and North American target markets with Glybera® for LPLD and for the next phases of development of the other programs currently in our pipeline. Our offices and laboratory space as well as our manufacturing facility and related equipment are leased under various operating and financial lease agreements (see also "Operating and Financial Overview – Contractual obligations").

# **Management and Employees**

#### General

Set out below is a summary of relevant information concerning our Board of Management, Supervisory Board, senior management team (the "Senior Management") and other employees. In addition, we set out a brief summary of certain significant provisions of Dutch corporate law and the Articles of Association in respect of our Board of Management and Supervisory Board.

### Management structure

The Company has a two-tier board structure, consisting of a Board of Management (*raad van bestuur*) and a Supervisory Board (*raad van commissarissen*).

The Board of Management is supported operationally by our Senior Management.

### **Board of Management**

### Powers, composition and function

The Board of Management is responsible for the day-to-day management of our operations under the supervision of the Supervisory Board. The Board of Management is required to keep the Supervisory Board in a timely manner informed in order to allow the Supervisory Board to carry out its task, 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 Board of Management may perform all acts necessary or useful for achieving our corporate purposes, save for those acts that are prohibited by law and/or by the Articles of Association. The Board of Management as a whole is authorized to represent us, as are any two members of the Board of Management acting jointly.

The Articles of Association provide that the number of members of the Board of Management will be determined by the Supervisory Board, and that the Board of Management will consist of one or more members. In the event that the Board of Management comprises two or more members, the Supervisory Board may attribute specific titles to individual members of the Board of Management, such as "Chief Executive Officer", "Chief Financial Officer", "Chief Operating Officer" and "Chief Scientific Officer".

Members of the Board of Management are appointed by the General Meeting of Shareholders following a non-binding proposal of the Supervisory Board. In view of the Dutch Corporate Governance Code, the Articles of Association provide that, unless provided otherwise in the resolution to appoint such member (i) members of the Board of Management are appointed for a maximum term of four years and (ii) a member of the Board of Management whose term of office expires, can be re-appointed immediately for a term of not more than four years at a time.

The General Meeting of Shareholders may suspend or dismiss members of the Board of Management at any time. The Supervisory Board may also suspend members of the Board of Management at any time. A suspension of a member of the Board of Management by the Supervisory Board may be discontinued at any time by the General Meeting of Shareholders.

Under the Dutch Civil Code, decisions of our Board of Management require approval by our General Meeting of Shareholders if and when these relate to an important change in the

identity or character of the Company or of our undertaking. Such decisions include in any case:

- a transfer of our undertaking, or practically the entire undertaking, to a third party;
- the entry into or termination, by ourselves or one of our subsidiaries, of (i) a long-term cooperation with another legal person or partnership or (ii) a general or limited partnership as a general partner, in each case only to the extent such would be of farreaching significance in respect of ourselves;
- the acquisition or divestment of an interest in the capital of another legal person or partnership as a participating holding (*deelneming*), within the meaning of the Dutch Civil Code, having a value of at least one-third of the aggregate amount of our assets according to our (consolidated) balance sheet and the explanatory notes thereto of our lastly adopted annual accounts.

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

- strategy issues, strategic long term policy plans and preconditions which are to be observed in respect of the strategy, for instance regarding the financial ratios;
- the operational and financial objectives of the Company;
- the sale or disposition by the Company of all, or an essential part of its assets;
- the issuance and acquisition of shares and of debentures chargeable against the Company or chargeable against a limited partnership (commanditaire vennootschap), or a general partnership (vennootschap onder firma) of which the Company is the fully liable partner;
- petition for quotation, or withdrawal of quotation from a price list of any stock exchange of shares and certain debentures;
- entering into or terminating long term co-operation by the Company or a dependent company with another legal entity, company, or with a limited partnership or general partnership of which the Company is the fully liable partner, if subject co-operation or termination of co-operation is of major significance to the Company;
- participating by the Company or a dependent company in the capital of another company
  for at least one fourth of the Company's issued capital plus the reserves according to its
  balance sheet and explanatory notes, as well as a significant increase or decrease of
  such participation;
- investments requiring an amount equal to at least one fourth of the Company's issued capital plus reserves, according to its balance sheet and explanatory notes;
- filing a petition for bankruptcy (faillissement) or for suspension of payments (surseance van betaling);
- the termination of the employment of a considerable number of the Company's or a dependent company's employees simultaneously or within a short period of time;

- a significant change in the employment conditions of a substantial number of the Company's or a dependent company's employees; and
- a proposal to decrease the Company's issued capital.

Our Supervisory Board may determine that, contrary to the above, a resolution that would otherwise be subjected to its approval, shall not require its approval if the amount involved does not exceed a value fixed by the Supervisory Board and notified to the Board of Management in writing. The Supervisory Board shall be entitled to require further resolutions of the Board of Management in addition to those listed above to be subject to its approval. Such further resolutions shall be clearly specified and notified to the Board of Management in writing. The absence of approval of the Supervisory Board shall not affect the authority of the Board of Management or its members to represent the Company.

Furthermore, the Board of Management 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 Board of Management**

The Board of Management is currently composed of the following members:

Name	Age	Position	Date of current appointment	Term
Jörn Aldag	50	Chief Executive Officer	4 November 2009	Up to the first General Meeting of Shareholders after 4 November 2013
Piers Morgan	44	Chief Financial Officer	28 April 2010	Up to the first General Meeting of Shareholders after 28 April 2014

The business address of both members of the Board of Management is Meibergdreef 61, 1105 BA Amsterdam Zuidoost, the Netherlands.

# Jörn Aldag (Chief Executive Officer)

Mr. Aldag was appointed by our General Meeting of Shareholders on 4 November 2009. Mr. Aldag graduated from the International Management European Business School in 1982 and followed the Advanced Management Program of the Harvard Business School. Mr. Aldag has over twenty five years of experience of executive, business and financial management, at Evotec AG in Germany, Molecular Partners AG in Switzerland, MAN AG and Treuhandanstalt both in Germany. As former President and CEO of Evotec AG, he was instrumental in transforming the company from a technology provider to one of the leading drug discovery and development companies in Europe. Mr. Aldag is currently Chairman of the Board of Molecular Partners AG and member of the supervisory board of the DESERTEC Foundation.

# Piers Morgan (Chief Financial Officer)

Mr. Morgan joined us as Chief Financial Officer in December 2009 and was appointed as member of our Management Board by our General Meeting of Shareholders on 28 April 2010. Mr. Morgan has ten years experience as CFO with biotechnology companies, including Phytopharm plc, BioAlliance Pharma SA, and Arrow Therapeutics Ltd. Prior to this period, he gained ten years experience in investment banking, working in Mergers & Acquisitions, and Equity Capital Markets with Close Brothers and Ernst & Young Corporate Finance. He qualified as a Chartered Accountant in London with PricewaterhouseCoopers.

#### **Supervisory Board**

#### Powers, composition and function

The Supervisory Board is responsible for supervising the management conducted by the Board of Management and our course of affairs and the business connected with it. The Supervisory Board shall assist the Board of Management by giving advice. In performing its duties, the Supervisory Board is required to act in the interests of our company and its associated business as a whole. The members of the Supervisory Board are not, however, authorized to represent us in dealings with third parties.

The Articles of Association provide that members of the Supervisory Board are appointed by the General Meeting of Shareholders following a non-binding proposal of the Supervisory Board. The number of Supervisory Board members is determined by the Supervisory Board itself.

In view of the Dutch Corporate Governance Code, the Articles of Association provide that members of our Supervisory Board will serve for a maximum of four years, unless provided otherwise in the resolution to appoint the Supervisory Board member concerned, and may only be reappointed twice. The General Meeting of Shareholders appoints a chairman and the Supervisory Board appoints a deputy chairman from amongst its members.

Under the Articles of Association, the General Meeting of Shareholders may suspend or dismiss Supervisory Board members at any time. The Articles of Association provide that the Supervisory Board members shall retire periodically in accordance with a rotation plan to be adopted 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 if the majority of the Supervisory Board members then in office are present or represented. The Supervisory Board may also adopt resolutions in writing or otherwise, *in lieu* of conducting an actual meeting, provided that any such resolutions are submitted to all members of the Supervisory Board in office at such time and provided further that no such member of the Supervisory Board objects to adopting resolutions without conducting a meeting. Each member of the Supervisory Board shall be entitled to cast one vote.

# **Members of the Supervisory Board**

The Supervisory Board is currently composed of the following members:

Name	Age	Position	Date of current appointment	Term
Ferdinand Verdonck	67	Chairman	25 April 2007	Up to the first General Meeting of Shareholders after 25 April 2011
Phillip van Holle	55	Member	16 April 2008	Up to the first General Meeting of Shareholders after 16 April 2012
Sander van Deventer	56	Member	28 April 2010	Up to the first General Meeting of Shareholders after 28 April 2014
Joseph Feczko	61	Member	20 September 2010	Up to the first General Meeting of Shareholders after 20 September 2014
Steven Holtzman	56	Member	20 September 2010	Up to the first General Meeting of Shareholders after 20 September 2014
François Meyer	62	Member	20 September 2010	Up to the first General Meeting of Shareholders after 20 September 2014

The business address of all members of our Supervisory Board is Meibergdreef 61, 1105 BA Amsterdam Zuidoost, the Netherlands.

#### Ferdinand Verdonck (Chairman)

Mr. Verdonck holds a law degree from the KU Leuven and degrees in economics from the KU Leuven and the University of Chicago. His professional experience is based on his work, mainly in financial services (Almanij and earlier with Lazard Frères) and also in manufacturing (Bekaert N.V.) From 1992 to 2003, he was the managing director of Almanij (now merged with its main subsidiary KBC). His responsibilities were primarily in the areas of the group's strategy, financial control, supervision of top management and governance and entailed board participation in publicly-traded and privately-held companies in many countries. Currently, he is chairman of Easdaq N.V., director of Galapagos N.V., J.P. Morgan European Investment Trust, Groupe SNEF, Laco Information Services and Phoenix Funds. Earlier he served as chairman of Banco Urquijo and director of Dictaphone Corporation Santens N.V. the Dutch Chamber of Commerce for Belgium and Luxemburg, Phoenix Investments Partners and Degussa Antwerpen N.V. Mr. Verdonck is a member of the General Council of the Vlerick Leuven Ghent Management School.

# Phillip van Holle (Member)

Mr. Van Holle has 30 years of marketing and sales experience in the pharmaceutical and biotechnology industries. Most notably he was responsible at Amgen Europe for the commercial roll-out of Neupogen® and Epogen®, the first two biotech blockbuster products. Subsequently he served as an executive at Genzyme Europe, overseeing the commercialization of Genzyme's orphan drugs. In 2005, he joined Celgene as Head of Celgene Europe. Over the past few years Celgene has grown into the fourth largest biotechnology company worldwide with a market capitalization of approximately \$20 billion.

#### Sander van Deventer (Member)

Professor Van Deventer, one of our co-founders, became a member of our Supervisory Board on 20 September 2009. From 5 July 2005 to 4 November 2009 he was a member of our Board of Management, holding the position of Chief Scientific Officer. As a consequence of our previous Chief Executive Officer Mr. Lorijn having left us as per such date for personal reasons, from 1 February 2009 until Mr. Aldag's appointment on 4 November 2009 Professor Van Deventer held the position of Chief Executive Officer on an interim basis.

Professor Van Deventer holds a degree in Medicine from the University of Amsterdam and obtained his Ph.D in 1988. He was chairperson at the Department of Gastroenterology of the AMC from 2002 to 2004, a director of the Anton Meelmeijer Center for Proteomics and Genomics of the AMC from 2003 to 2004 as well as venture partner of ABN AMRO Capital Life Sciences from 2004 to 2006. Professor Van Deventer is currently a Professor of Experimental Medicine at the AMC. He is also a board member of Argos Therapeutics Inc. and Borean Pharma and a partner of Forbion Capital Partners, the investment manager of one of our major shareholders, in which capacity he acts as chairperson of the Expert Panel of Forbion Capital Partners. Professor Van Deventer contributed to over 350 articles to renowned magazines in the field of medicine.

As a result of Professor van Deventer's previous position as a member of the Board of Management and because he is a partner of Forbion Capital Partners – the investment manager of one of our major shareholders -, he is not independent within the meaning of best practice provision III.2.2 of the Dutch Corporate Governance Code.

#### Joseph Feczko, M.D. (Member)

Dr. Feczko was, until May 2009, Senior Vice President and Chief Medical Officer (CMO) of Pfizer, Inc., and a member of the Executive Leadership Team with global responsibilities for all aspects of the company's medical, regulatory and safety activities. Following a time in private practice, he joined Pfizer in 1982 in New York. He then worked for ten years in the United Kingdom for both Pfizer and Glaxo where his responsibilities included supervising clinical research, regulatory affairs, data management and safety reporting. He returned to Pfizer in New York in 1996, where he held positions of increasing responsibility in clinical research, and regulatory affairs and safety, culminating in the role of CMO.

Mr. Feczko currently holds supervisory directorships with Cardoz Pharmaceuticals AB (chairman), and with Keryx Biopharmaceuticals, Inc. Dr. Feczko is currently a member of the Board of Directors of the Foundation for the National Institutes of Health, Research!America, the International Longevity Center, and the New York Academy of Medicine. He is a member of the Board of Directors of the Accordia Global Health Foundation and the Technical Expert Committee for the International Trachoma Initiative of the Task Force for Global Health. He is also a member of the Governing Board of the Technology Strategy Board of the United Kingdom.

Dr. Feczko is board-certified in Internal Medicine and a specialist in Infectious Diseases. He has a B.Sc. degree from Loyola University Chicago, and an M.D. from the University of Illinois of Medicine.

#### Steven Holtzman (Member)

Mr. Holtzman is a highly experienced biotech entrepreneur, who has founded and led a number of life sciences companies. He also has substantial experience in building collaborations with major pharmaceutical companies and licensing products. From 1996 to 2001, Mr. Holtzman served as a Presidential Appointee to the United States National Bio ethics Advisory Commission, the principal advisory body to the President and Congress on ethical issues in the biomedical and life sciences.

Mr. Holtzman served as Chief Executive Officer of Infinity Pharmaceuticals, Inc, 2006 to 2009 and as President from 2007 to 2008. Mr. Holtzman was also a co-founder of Infinity Discovery, Inc. and served as its Chief Executive Officer and as Chair of its board of directors from inception in 2001 until the time of its merger with Infinity Pharmaceuticals' predecessor company in 2006. Mr. Holtzman also served as President of Infinity Discovery from 2001 to 2006. From 1994 to 2001, Mr. Holtzman served as Chief Business Officer of Millennium Pharmaceuticals, Inc., a publicly traded pharmaceutical company. Prior to joining Millennium Pharmaceuticals, Inc., from 1986 to 1994, Mr. Holtzman was a founder and Executive Vice President of DNX Corporation, a publicly traded biotechnology company.

Mr. Holtzman currently holds supervisory directorships with Infinity Pharmaceuticals, Inc., as chairman and Anadys Pharmaceuticals Inc. as director, Sartori Pharmaceuticals, Inc. as director.

Mr. Holtzman graduated from Michigan State University and received his B.Phil. from Oxford University, which he attended as a Rhodes Scholar.

# François Meyer (Member)

Dr. Meyer was General Director for Research and Development at Aventis Pharma until 2002 and subsequently Director-General of Aventis' Gene Therapy Division, Gencell until his retirement in 2006. He joined Gencell as Vice-President in 1996, within the Rhône-Poulenc Group, prior to the formation of Aventis when Rhone-Poulenc merged with Hoechst. He was promoted to Vice President of RPR Global Research in 1997, and Corporate Senior Vice President of Global Research in 1998.

Previously, in 1992, Dr. Meyer headed Sandoz Pharma's gene and cell therapy business as Vice President, where he also served as a member of the company's Corporate Research Board. From 1989 - 1992, he was Director of Research at the CNRS. From 1980 to 1984, Dr. Meyer built and headed the Molecular Genetics department in the newly formed Biotechnology division at Ciba- Geigy, where he was responsible for the discovery of new recombinant proteins.

Mr. Meyer holds supervisory directorships with BioSeek Inc., Urogene SA, Introgen Therapeutics, Inc., Gene Therapy, Inc. In addition he is member of the Scientific Advisory Boards of Genethon, Systemix, Inc. and Biotransplant, Inc.

He graduated from the Swiss Federal Institute of Technology, in Zurich, and studied Biochemistry and Molecular Biology at the University of Zurich. He received his Ph.D. from the Institute for Molecular Biology in 1978, and afterwards became a Senior Member at the Institute. During his career, Dr. Meyer has also served as a lecturer in Molecular Biology at the Swiss Federal Institute of Technology.

# **Supervisory Board committees**

Our Supervisory Board has appointed from among its members an Audit Committee and a Remuneration and Nominating Committee.

#### **Audit Committee**

The Audit Committee consists of Mr. Verdonck as chairperson and financial expert and Mr. van Holle and Mr. van Deventer as members. The Audit Committee makes recommendations to the Supervisory Board regarding audit, financial and related issues. The supervision of the Audit Committee includes, but is not limited to, the following activities of the Board of Management:

- the operation of our internal risk management and control systems, including supervision
  of the enforcement of the relevant legislation and regulations, and supervising the
  operation of codes of conduct;
- the provision of our financial information (choice of accounting policies, application and assessment of the effects of new rules, information about the handling of estimated items in the annual accounts, forecasts, work of internal and external auditors, etc.);
- our compliance with recommendations and observations of internal and external auditors;
- the role and functioning of our internal audit department;
- our policy on tax planning;
- our relations with the external auditor, including in particular such auditor's independence, remuneration and any non-audit services;
- · our financing; and
- application of information and communication technology.

Furthermore, the Audit Committee shall act as the principal contact for the external auditor if it discovers irregularities in the contents of the financial reports and meet with the external auditor as often as it considers necessary, but at least once a year, without members of our Board of Management being present.

The duties of the Audit Committee are defined by the Audit Committee Regulations, which are published on our website.

#### Remuneration and Nominating Committee

Chairman of the Remuneration and Nominating Committee is Holtzman, with the other members being Mr. Feczko and Mr. Meyer. The Remuneration and Nominating Committee makes recommendations to the Supervisory Board on salaries and incentive compensation for our employees, including the Board of Management, as well as on remuneration of the individual members of the Board of Management and the Supervisory Board. The tasks of the Remuneration and Nominating Committee include, but are not limited to:

 drawing up selection criteria and appointment procedures for members of our Board of Management and our Supervisory Board;

- periodically assessing the size and composition of our Board of Management and our Supervisory Board, and making a proposal for a composition profile of the Supervisory Board;
- periodically assessing the functioning of individual members of our Board of Management and our Supervisory Board, and reporting on this to the Supervisory Board;
- making proposals for appointments and reappointments; and
- supervising the policy of our Board of Management on the selection criteria and appointment procedures for our Senior Management.

The duties of the Remuneration and Nomination Committee are defined by the Remuneration and Nomination Committee Regulations, which are published on our website.

#### **Senior Management**

Our Board of Management is supported by the Senior Management. Our Senior Management is currently composed of the following members:

Mark Chadwick (Patent Counsel)

Dr. Chadwick joined us in November 2008 as Patent Counsel. He holds a degree in Natural Sciences from the University of Cambridge and a Ph.D in Genetics from the University of East Anglia. Before joining us, Dr. Chadwick qualified as a European Patent Attorney at J. A. Kemp and Co., where he spent 9 years. He then worked as a European Patent Attorney for DSM, advising on their Food Specialties and White Biotechnology businesses.

Monique Marelis (Director Human Resources )

Ms. Marelis joined us in August 2008 as Director Human Resources. She holds an MBA from Kingston University in London. Prior to joining us, Ms. Marelis worked at Dell, where she spent five years working as Manager Human Resources. Prior to joining Dell, Ms. Marelis worked as an HR consultant on a range of national and international projects, providing interim, consultancy and project services.

Claudia Meyer (Director Regulatory Affairs)

Dr. Meyer joined us in September 2010 as Director Regulatory Affairs. She holds a MSc in Microbiology, Genetics and Biochemistry and a Ph.D in Microbiology and Immunology from the University of Bonn. Prior to working with us, Dr. Meyer spent six years with Human Genome Sciences Europe, working in Regulatory Affairs as a Senior RA Manager responsible for European development of biotechnological products in autoimmune disease, oncology and hepatitis C. Prior to that she was responsible for a part of CSL Behring's product portfolio for more than three years in Regulatory Affairs. She is also vice-chair of the BioManufacturing Working Group of the European Biopharmaceutical Enterprises, a specialized group of EFPIA.

Harald Petry (Director of Research and Development)

Dr. Petry joined us in May 2007 and has been Director Research since 2008. Currently he is the Director of Research and Development. He has worked in the area of gene therapy for more than 15 years and has extensive experience in pharmaceutical research. After his Ph.D he built up a career in academic research. Before joining us, Dr. Petry worked at Jenapharm

GmbH and Berlex Biosciences in different functions with increasing managerial and leadership responsibility.

Hans Preusting (Operations and Project Management)

Dr. Preusting joined us in August 2006 as Director Process Development and Manufacturing. In December 2009 Dr. Preusting became responsible for Operations and Project Management. Dr. Preusting holds a Ph.D in Chemistry and has over 14 years of experience in the production process of biologicals. He worked at DSM Biologics as Interim Engineering Manager, Senior Project Manager and Operations Manager from 1999 to 2003. He also was a director of influenza and Cell Culture Vaccine Manufacturing at Solvay Pharmaceuticals B.V. from 2003 to 2006. As such, he set up a new production organization for a green field cell culture based Influenza vaccine manufacturing facility and as of 2006 he was also responsible for the existing egg-based vaccine manufacturing facility. Dr. Preusting holds two patents and has published over twenty scientific articles.

# Tamara Tugal (Business Development Director )

Dr. Tugal joined us in June 2008 and is responsible for business development activities within the company, including business strategy and deal flow. Dr. Tugal holds a BSc in Molecular Biology from the University of Edinburgh, a Ph.D in Biochemistry from University College London, conducting research under the supervision of Sir Tim Hunt (Nobel Prize for Medicine, 2001), and holds an MBA from London Business School. Prior to AMT, Dr. Tugal worked in the field of drug discovery and development in the UK, where she held business and managerial roles at Lorantis Ltd and at Eden Biodesign Ltd.

#### Arnold Vroege (Director Quality Assurance and Quality Control)

Mr. Vroege joined us in January 2007 as Director Quality Assurance and Quality Control and he currently is Director Quality Assurance. He holds a degree in Pharmacy from the University of Groningen. He was Head of the QA Department at the Foundation for the Advancement of Public Health and Environmental Protection (SVM) from 2000 to 2003 and acquired extensive experience with biologicals at Solvay Pharmaceuticals where he worked as QA Manager from 2003 to 2005 and as Head QA/QC in 2006. Mr. Vroege is a member of the Dutch Industry Pharmacists (NIA), the Dutch Association of Research Quality Assurance (DARQA) and the Group Quality Assurance Pharmaceutical Industry (GFKI).

# Janneke de Wal (Director Global Marketing and Sales)

Dr. De Wal has over 20 years of experience in marketing, sales and product development, including the introduction of orphan drug products. Her experience encompasses a wide range of international positions in Genzyme, Yamanouchi Pharma and other companies.

The business address of all members of our Senior Management is Meibergdreef 61, 1105 BA Amsterdam Zuidoost, the Netherlands.

# Remuneration of the Board of Management, the Supervisory Board and Senior Management

#### Remuneration of the Board of Management

According to the Articles of Association, our General Meeting of Shareholders adopts the remuneration policy in respect of the remuneration of our Board of Management. Our Supervisory Board establishes the remuneration of the individual members of our Board of Management, taking into account the policy adopted by our General Meeting of Shareholders,

provided that arrangements in the form of (depositary receipts for) shares or rights to subscribe for (depositary receipts for) shares are subject to the approval of our General Meeting of Shareholders. Such a proposal must include the number of (depositary receipts for) shares or rights to subscribe for (depositary receipts for) shares that may be granted to the members of the Board of Management and which criteria apply to a grant or modification.

Our current remuneration policy is aimed to attract, motivate and retain members of the Board of Management of the highest caliber - management with an international background that is essential to the successful leadership and effective management of a young and fast-growing biotechnology company with the ambition to be a world leader in gene therapy.

Pursuant to the current remuneration policy, the members of the Board of Management are rewarded accordingly and their compensation comprises both fixed and variable components. The variable remuneration components are designed to reflect the achievement of predetermined operational and strategic objectives.

The compensation of the Board of Management comprises three time-frames:

- Short-term compensation, consisting of base salary and bonus
- · Long-term compensation, consisting of depository receipts for shares, and
- Retirement compensation, pension.

The current remuneration policy was last amended by the General Meeting of Shareholders held on 15 April 2009 (consequently prior to the appointment of the current members of the Board of Management in November 2009 (Jörn Aldag) and April 2010 (Piers Morgan)).

#### Remuneration of the Supervisory Board

The remuneration of the members of the Supervisory Board is determined by the General Meeting of Shareholders.

The table below provides an overview of the annual remuneration of the Supervisory Board.

	Annual remuneration in €	Attendance fee: in person / by telephone
Ferdinand Verdonck	30,000	1,500 / 500
Phillip van Holle	20,000	1,500 / 500
Sander van Deventer	20,000	1,500 / 500
Joseph Feczko	20,000	1,500 / 500
Steven Holtzman	20,000	1,500 / 500
François Meyer	20,000	1,500 / 500

# Total remuneration paid in relation to financial year 2009

The total remuneration we paid to or for the benefit of members of our Board of Management, our Supervisory Board and our Senior Management in relation to the financial year 2009 amounted to approximately €2,714,000. The following table denotes the breakdown in the remuneration in relation to the financial year 2009 of the members of the Board of Management, the Supervisory Board and Senior Management.

Name	Salary	Bonus	Share based payments	Pension	Advisors fee	Total			
			€ '000						
Board of Man	Board of Management <sup>(1)</sup>								
Jörn Aldag	81	-	314	10	-	405			
Sander van Deventer <sup>(2)</sup>	-	-	-	-	213	213			
Ronald Lorijn <sup>(3)</sup>	52	174	-	240	-	466			
Supervisory E	Board <sup>(4)</sup>								
Ferdinand Verdonck	40	-	-	-	-	40			
George Morstyn <sup>(5)</sup>	25	-	-	-	-	25			
Phillipe van Holle	27	-	-	-	-	27			
Alexander Ribbink <sup>(6)</sup>	30	-	-	-	-	30			
Senior Management									
Senior Management	1,039	302	13	154	-	1,508 <sup>(7)</sup>			
Total	1,294	476	327	404	213	2,714			

<sup>(1)</sup> As he was appointed as a member of our Board of Management in 2010, this table does not include remuneration details of our Chief Financial Officer, Piers Morgan.

<sup>(2)</sup> In 2009 Professor Van Deventer was seconded to us by Forbion Capital Partners Management Services B.V. In addition, he provided consultancy services to us on a regular basis pursuant to a consultancy agreement (see also "Related Party Transactions – Forbion Capital Partners). Professor Van Deventer ceased to be a member of our Board of Management on 4 November 2009 and he was appointed to our Supervisory Board on 28 April 2010.

<sup>(3)</sup> Mr. Lorijn, our former Chief Executive Officer, left us as per 1 February 2009.

<sup>(4)</sup> As they were appointed as members of our Supervisory Board in 2010, this table does not include remuneration details of Professor Van Deventer, Mr. Feczko, Mr. Holtzman and Mr. Meyer for their membership of the Supervisory Board.

<sup>(5)</sup> Mr. Morstyn ceased to be a member of our Supervisory Board on 20 September 2010.

<sup>(6)</sup> Mr. Ribbink ceased to be a member of our Supervisory Board on 28 April 2010.

<sup>(7)</sup> This amount includes certain termination payments made in respect of former members of our Senior Management, and does not include the remuneration of Dr. Claudia Meyer, who joined us in 2010.

# **Equity holdings**

The table below sets forth the number of options to acquire shares and depositary receipts as well as the current number shares and depositary receipts owned by members of our Board of Management, our Supervisory Board and our Senior Management:

Name	Shares	Options to acquire shares <sup>(1)</sup>	Depositary receipts for shares	Options to acquire depositary receipts for shares	
Board of Man	agement				
Jörn Aldag	-	131,400	110,000	73,000 <sup>(2)</sup>	
Piers Morgan	-	87,600	-	40,000 <sup>(3)</sup>	
Supervisory E	Board				
Ferdinand Verdonck	-	-	52,799	-	
Phillipe van Holle	-	-	30,000	-	
Sander van Deventer	47,163	-	131,820	10,000 <sup>(4)</sup>	
Joseph Feczko	-	-	30,000 <sup>(5)</sup>	-	
Steven Holtzman	-	-	30,000 <sup>(5)</sup>	-	
François Meyer	-	-	30,000 <sup>(5)</sup>	-	
Senior Manag	gement				
Mark Chadwick	-	62,050	-	-	
Monique Marelis	-	62,050	500	-	
Claudia Meyer	-	62,050	-	-	
Harald Petry	-	73,000	3,137	-	
Hans Preusting	-	73,000	12,068	-	
Tamara Tugal	-	62,050	409	-	
Arnold Vroege	-	47,450	12,200 <sup>6</sup>	-	
Janneke de Wal	-	62,050	400	-	
Total	47,163	722,700	443,333	123,000	

<sup>(1)</sup> All options to acquire shares were granted in 2010 and will expire in 2020. The exercise price of the options varies between €1,95 and €2.97. All options to acquire shares have been granted under the Stock Option Plan.

- (2) In addition to the 110,000 depositary receipts for shares Mr. Aldag holds, Mr. Aldag, may be granted the option to acquire up to 73,000 additional depository receipts for shares at 10% of the average closing price of the shares at Euronext Amsterdam on the five business days prior to the date of grant upon achievement of certain defined Company objectives within the first year of employment. Anti dilution protection will apply to the 183,000 depositary receipts for shares.
- (3) The option to acquire 40,000 depository receipts for shares at 10% of the average closing price of the shares at Euronext Amsterdam of the five business days prior to the day of grant may be granted upon Mr. Morgan raising an amount of at least €15 million from external fundraisers within the first years of employment.
- (4) Upon continued advice by Professor Van Deventer to us in the years 2010 and 2011, Professor Van Deventer will be granted 5,000 depositary receipts for shares under the Share Incentive Plan in the year 2010 and 2011.
- (5) Following the first anniversary of the appointment as member of the Supervisory Board, 30,000 options to acquire shares will be granted under the Stock Option Plan to this member of the Supervisory Board.
- (6) Of the 12,200 depositary receipts for shares 200 depositary receipts for shares are part of an undivided inheritance with five legal heirs of which Mr. Vroege is one.

The depositary receipts for shares have been granted under the Share Incentive Plan, which is further described below.

The options to acquire shares have been granted under the Stock Option Plan, which is further described below.

#### **Equity incentive plans**

Our employee remuneration system is divided into a base salary plus a variable bonus or incentive. To achieve both short and long term inventive we operate the following equity incentive plans.

#### Share Incentive Plan

We operate a share-based payment plan (the "Share Incentive Plan"). Under the Share Incentive Plan, our Board of Management has the discretion to award depositary receipts for shares to our employees, including Senior Management, and our Supervisory Board has the discretion to award such depositary receipts to members of our Board of Management, in each case subject to the overriding general authority of our Supervisory Board to amend or otherwise alter the terms of the Share Incentive Plan. The depositary receipts for shares granted under the Share Incentive Plan are granted at 90% discount of the average closing price of our shares at Euronext Amsterdam on the five days prior the date of grant and have a three-year vesting period. At the date of this Prospectus 624,440 depositary receipts for shares are outstanding under the Share Incentive Plan.

The depositary receipts under the Share Incentive Plan are issued by a foundation, Stichting Participatieregeling AMT (the "**Depositary**"). This foundation holds legal title to the underlying shares (see also "Description of Share Capital and Corporate Governance – Share capital – Depositary receipts").

The depositary receipts have a fair market value equal to the market value of the underlying shares they represent. Upon the Depositary's acceptance of the exercise of a sale option by a participant, the Depositary (or its designee) will have to pay the fair market value of the depositary receipts to such participant.

The Depositary has a repurchase option which may be exercised, *inter alia*, upon the relevant participant being adjudicated bankrupt or upon certain events occurring in respect of ourselves (e.g. a merger or the sale of (substantially) all of our assets). The participant may not decline to sell his depositary receipts. Depending on the reason for exercising the

repurchase option, the participant is considered to be a good leaver, a voluntary leaver or a bad leaver respectively and the Depositary will be required to pay to the relevant participant the fair market value, the original purchase price or the par value of such depositary receipts respectively.

We previously also operated a cash-settled stock option plan. The last option grants under this plan were made in 2004 and since then all outstanding options under the plan have either lapsed or been exercised.

# Stock Option Plan

We operate a stock option plan ("Stock Option Plan") which was approved by our General Meeting of Shareholders on 28 April 2010. Under the Stock Option Plan the Board of Management, subject to approval of the Supervisory Board may grant options to acquire shares to certain of our employees. The exercise price of the options is the trading price of our shares on closing on the date of grant. The number of shares under option shall not exceed 10% of our issued share capital. The Board of Management may amend the terms and conditions of the Stock Option Plan.

The options granted are subject to the following vesting period:

- 50% of the options vest after a 3 year period, subject to meeting a performance condition at the end of the 3 year period that our share price shall have increased by 50% over the period;
- 25 % of the options vest after a 4 year period, subject to meeting a performance condition at the end of the 4 year period that our share price shall have increased by 75% over the period; and
- The remaining 25% of the options vest after a 5 year period, subject to meeting a performance condition at the end of the 5 year period that our share price shall have increased by 100% over the period.

Options to acquire shares that have vested can only be exercised if (i) the employee is not in the possession of inside information and (ii) outside the closed period en (iii) if the option has not lapsed.

If in any year the options miss the hurdle applicable to vesting, then these options shall be retested in the subsequent two years at the then prevailing hurdle rate, but any unvested options (being options that have not met the vesting criteria) shall lapse after 5 years.

#### Matched Reinvestment Plan

Through our 'Matched Reinvestment Plan' we offer employees the opportunity to convert their incentive payment in to shares. Under the terms of the Matched Reinvestment Plan we will match the employee's investment in shares by granting options to acquire shares equal in number to the investment made by the employee.

All employees are eligible for the Matched Reinvestment Plan and can invest 100% or 50% of their incentive into our shares.

#### Other information

None of the members of the Board of Management, Supervisory Board and Senior Management is, or has been, (i) subject to any convictions in relation to fraudulent offences in the last five years, (ii) in the last five years associated with any bankruptcies, receiverships or liquidations of any entities in which such members held any office, directorships or senior management positions, or (iii) subject to 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.

#### Administrative, management and supervisory bodies conflicts of interest

Other than the fact that our Supervisory Board member Professor Van Deventer is a partner of Forbion Capital Partners, the investment manager of one of our major shareholders, and except as disclosed in "Related Party Transactions", there are no potential conflicts of interest between the private interests or other duties of the members of our Board of Management, Supervisory Board or Senior Management and their duties and responsibilities to us.

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

# **Employment agreement of the members of the Board of Management**

Jörn Aldag

Mr. Aldag has an employment agreement with us for period of four years, subject to termination upon eight months' notice should we terminate and four months' notice should Mr. Aldag terminate. The agreement provides for a base salary of €320,000 per annum (excluding 8% holiday allowance) plus a bonus with a maximum of 30% of the base salary to be paid out in cash or in depositary receipts for shares, at the election of Mr. Aldag. The bonus is conditional upon reaching targets agreed upon annually with the Remuneration Committee of the Supervisory Board. In addition Mr. Aldag receives a travel allowance of €27,000 per annum.

Mr. Aldag has been granted the right to purchase 110,000 depositary receipts for shares under the terms and conditions of the Share Incentive Plan. Subject to certain conditions Mr. Aldag has the option to acquire an additional 73,000 depositary receipts for shares under the same conditions. In the event of a capital increase we will grant Mr. Aldag such number of additional depositary receipts for shares to safeguard his position prior to such dilutive event.

In the event of a new controlling shareholder of the Company deciding not to maintain Mr. Aldag in a function at least equivalent to his current one, Mr. Aldag has the right to leave us within two months. In such case pay of the monthly based salary and holiday allowance will continue for a period of eighteen months starting on the day of termination and ending on the date at which Mr. Aldag enters into a substantial new employment. This compensation shall replace all claims Mr. Aldag may have with regard to us in relation to the termination of the employment agreement.

Mr. Aldag is subject to a non-competition covenant for a period of six months following the termination of his employment.

# Piers Morgan

Mr. Morgan has an employment agreement with us for period of four years, subject to termination upon four months' notice should we terminate and two months' notice should Mr. Morgan terminate. The agreement provides for an initial base salary of €192,000 per annum (excluding 8% holiday allowance) plus a bonus with a maximum of 30% of the base salary conditional upon reaching targets set by our Chief Executive Officer and a travel allowance of €15,000 per annum. The base salary of Mr. Morgan shall be raised to €207,000 per annum, if he raises external funding of at least €15 million in his first year of his employment with us.

Subject to certain conditions Mr. Morgan has been granted the right to purchase 40,000 depositary receipts for shares at a price of 10% of the average closing price of our shares at Euronext Amsterdam on the five days prior the date of grant.

Mr. Morgan is subject to a non-competition covenant for a period of twelve months following the termination of his employment.

#### Severance payments

Except for Mr. Aldag's agreement as set out in "Employment agreement of the members of the Board of Management", the employment agreements with the members of our Board of Management, the Supervisory Board and Senior Management do not provide for severance payments in the event of termination.

# Director's and officer's insurance and indemnity

Under Dutch law, members of Board of Management and the Supervisory Board may be liable to us for damages in the event of improper or negligent performance of their duties. They may be jointly and severally liable for damages to us and to third parties for infringement of the Articles of Association or of certain provisions of the Dutch Civil Code. In certain circumstances, they may also incur additional specific civil and criminal liabilities. Members of the Board of Management, the Supervisory Board, the Senior Management and certain other officers of the Company are insured under an insurance policy against damages resulting from their conduct when acting in the capacities as such members or officers.

The insurance policy is governed by the laws of the Netherlands and covers financial loss (including defense cost, see below) up to €20,000,000. Under this policy, the members of our Board of Management and Supervisory Board are insured against any claim made against them and wrongful acts committed by them in their respective capacities. The insurance policy has global coverage.

Furthermore, we provide indemnification for members of our Board of Management and Supervisory Board against 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 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 Board of Management 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

The current pension plan provides for a collective pension scheme for our employees as of the age of 20. This pension scheme is insured with a large insurance company in the Netherlands. The pension scheme applied is defined contribution based. The contribution increases depending on the age of the employee, such in accordance with the defined contribution tables set by the Dutch Tax Authorities. Except for an employee contribution of 6.1% of the pensionable salary, the costs of this pension scheme are for our account. All employees participate in this collective pension scheme. For the year 2009 the pension costs for the pension plan amounted to €239,000.

#### **Employees**

On the date of this Prospectus we have 81 employees. In full-time equivalent (FTE) they are classified as follows: 12.9 FTEs in our department of Management and Support and 64.9 in our department of Research and Development.

In addition we employ a varying number of temporary employees, for the year 2009 on average between 5 and 10 temporary employees were employed.

At the end of 2007, 2008 and 2009, we had 58, 90 and 83 employees, respectively.

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# **Major Shareholders**

The following table shows details of the persons other than members of our Board of Management and Supervisory Board who, as at the date of this Prospectus (5 October 2010, 00:00 CET) and as far as we are aware, have a direct or indirect capital or voting interest in Amsterdam Molecular Therapeutics (AMT) Holding N.V. that needs to be disclosed under Dutch law.

The information in this table is based on the AFM kept public register of all notifications made pursuant to the Financial Supervision Act and the Decree on the Disclosure of Major Holdings and Capital Interests in Securities-Issuing Institutions (*Besluit melding zeggenschap en kapitaalbelang in uitgevende instellingen*). For an overview op applicable notification requirements see "Description of Share Capital and Corporate Governance-Notification of holdings of voting rights and capital interest".

The number of shares or voting rights as well as the percentage of shares or voting rights held by these parties at the date of Prospectus may be different.

Name	# of shares	# of voting rights	% of shares	% of voting rights	Capital interest <sup>(5)</sup>	Voting interest <sup>(6)</sup>	Type of security
Coöperatieve AAC LS U.A. (1)	2,237,686	2,237,686	16.06	16.06	Actual	Actual	Shares
Advent Venture Partners LLP <sup>(2)</sup>	2,143,967	2,143,967	15.39	15.39	Actual	Actual	Shares
Coöperatieve Gilde Healthcare II U.A. (3)	2,037,686	2,037,686	14.63	14.63	Actual	Actual	Shares
Crédit Agricole Private Equity <sup>(4)</sup>	1,118,842	1,118,842	8.03	8.03	Actual	Actual	Shares
Forbion Co-Investment Coöperatief U.A.	1,099,744	1,099,744	7.49	7.49	Potential	Potential	Convertible loan note

- (1) An investment fund managed by Forbion Capital Partners.
- (2) An investment fund managed by Advent Venture Partners
- (3) An investment fund managed by Gilde Healthcare Partners.
- (4) An investment fund managed by Crédit Agricole.
- (5) An "actual capital interest" concerns shares in respect of which the holder of a substantial holding holds actual disposal (section 5:33(1) sub b under 1° and 2° of the Financial Supervision Act). A "potential capital interest" concerns an interest that a holder of a substantial holding is considered to hold on the basis of an option or other agreement (section 5:33(1) sub b under 4° of the Financial Supervision Act).
- (6) An "actual voting interest" concerns votes in respect of which the holder of a substantial holding holds actual disposal (section 5:33(1) sub d of the Financial Supervision Act). A "potential voting interest" concerns an interest that a holder of a substantial holding is considered to hold on the basis of an agreement (section 5:33(1) sub d of the Financial Supervision Act).

Except as disclosed above, we are not aware of any other person or legal entity who, as per the date of this Prospectus, has a direct or indirect capital or voting interest in Amsterdam Molecular Therapeutics (AMT) Holding N.V. of 5% or more. None of the parties listed above has voting rights which are different from other holders of our shares. Each share entitles the holder thereof to one vote at the General Meeting of Shareholders

We are not aware of any party, or any parties acting in concert, that directly or indirectly control the vote at any General Meeting of Shareholders, nor are we aware of any arrangement the operation of which may result in a change of control of Amsterdam Molecular Therapeutics (AMT) Holding N.V.

# **Related Party Transactions**

# Forbion Capital Partners

Forbion Capital Partners has an interest in Amsterdam Molecular Therapeutics (AMT) Holding N.V. in excess of 10%. In addition, Professor Van Deventer, who served as our interim Chief Executive Officer from February to November 2010 and currently serves as member of our Supervisory Board, is a partner of Forbion Capital Partners. As a consequence, Forbion Capital Partners is a related party to us.

In 2008 and 2009, Professor Van Deventer was seconded to us by Forbion Capital Partners Management Services B.V. Furthermore, since 2008 though the date of this Prospectus he has served as a consultant. The total remuneration paid to Professor Van Deventer during 2007, 2008 and 2009 amounted to €442,000, €171,000 and €213,000 respectively. In relation to his services during the six month period ending 30 June 2010, Professor Van Deventer received a total of €47,000 in respect of his services.

In 2009, as part of the arrangements relating to the convertible loan notes we issued on 22 December 2009 (see "Description of Share Capital and Corporate Governance – Convertible loan notes), we have reimbursed the legal costs of Forbion Capital Partners of €20,000.

# Academic Medical Centre of the University of Amsterdam

Up to 31 October 2008, the AMC was a related party to us.

In 2007 and 2008, we used various services from the AMC and its subsidiaries, including use of testing services, maintenance, IT assistance, research and other services. In addition, we entered into various operating lease contracts with the AMC and its subsidiaries. The total expenses amounted to €397,000 in 2007 and €147,000 in 2008. In 2007, following our initial public offering, we repaid a convertible loan we had received in 2005 from a subsidiary of the AMC.

#### Board of Management, Supervisory Board and Senior Management

The remuneration paid to member of the Board of Management, Supervisory Board and Senior Management are set out in detail in "Management and Employees".

#### Other

In 2007 and 2008, we used services from relatives of our Chief Executive Officer at the time, Mr. Lorijn, in the area of corporate communications for a total amount of €29,000 in 2007 and €49,000 in 2008.

Further information of these transactions between us and related parties (other than transactions with our subsidiaries) during the period covered by the historical financial information included in this Prospectus can be found in the following parts of our historical consolidated financial statements incorporated by reference in this Prospectus.

Related party transactions in 2007

Note 10 (Loan from related party) and 26 (Related-party transactions) of the notes to the audited consolidated financial statements for the year 2007

Related party transactions in 2008 Note 23 (Related-party transactions) of the

notes to the audited consolidated financial

statements for the year 2008

Related party transactions in 2009 Note 23 (Related-party transactions) of the

notes to the audited consolidated financial

statements for the year 2009

Related party transactions in first six months Note 14 (Related party transactions) of the

of 2010

selected notes to the unaudited condensed interim financial report for the six months

ended 30 June

# **Description of Share Capital and Corporate Governance**

#### General

Amsterdam Molecular Therapeutics (AMT) Holding N.V. is a public limited liability company (naamloze vennootschap) under the laws of the Netherlands. The company was originally incorporated on March 20, 1998 under Dutch law as Amsterdam Molecular Therapeutics (AMT) B.V. That name was subsequently changed into Amsterdam Molecular Therapeutics (AMT) Holding B.V., effective as of 5 June 2007. As of that date, the intellectual property activities and other activities (such as production and research & development) were transferred to two separate companies by means of a statutory demerger (afsplitsing) of these activities into two newly incorporated private companies with limited liability (besloten vennootschappen met beperkte aansprakelijkheid), named Amsterdam Molecular Therapeutics (AMT) B.V. These companies are both wholly-owned subsidiaries of the Company which was renamed Amsterdam Molecular Therapeutics (AMT) Holding N.V. following the amendment of its articles of association on 20 June 2007.

In this chapter references to us "we", "our", "us" and similar terms refer to Amsterdam Molecular Therapeutics (AMT) Holding N.V. only.

We are registered with the Trade Register of the Chamber of Commerce for Amsterdam, the Netherlands under number 33301321. Our corporate seat is in Amsterdam, the Netherlands and our office address is Meibergdreef 61, 1105 BA, Amsterdam Zuidoost, the Netherlands. We can be contacted by telephone on + 31 (0)20 5667394 and by fax on +31 (0)20 5669272.

Our articles of association were last amended by deed of amendment, executed on 29 September 2010 before a deputy of D.F.M.M. Zaman, civil law notary in Rotterdam, the Netherlands.

Set out below is a summary of relevant information concerning our share capital and corporate governance together with a brief summary of certain provisions of the Articles of Association.

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

#### **Corporate objects**

Pursuant to Article 3 of the 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 research, development, commercialization and production of unique technology relating to virus-based therapeutic products and vaccines;
- to develop and trade in patents, trade marks, licenses, know-how and other intellectual property rights;

- to render advice and services to businesses and companies with which we form a group and to third parties;
- to borrow, to lend and to raise funds, including the issue of bonds, promissory notes
  or other securities or evidence of indebtedness, as well as to enter into agreements in
  connection with the aforementioned activities;
- to grant guarantees, to bind ourselves and to pledge our assets for obligations of businesses and companies with which we form a group and on behalf of third parties;
- to acquire, dispose of, manage and exploit registered property and items of property in general; and
- to do all that is connected therewith or may be conducive thereto, all to be interpreted in the broadest sense.

# Share capital

# Authorized and issued share capital

At the date of this Prospectus, our authorized capital amounts to €1,300,000 divided into 32,500,000 shares with a nominal value of €0.04 each. At the date of this Prospectus, and consequently prior to the issue of any New Shares, our issued and outstanding share capital as of the date of this Prospectus amounts to €602,749.12 consisting of 15,068,728 shares with a nominal value of €0.04 each, all fully paid up and created under Dutch law.

At the date of this Prospectus we do not hold any of our shares.

#### History of share capital

The table below provides details on our authorized and issued and outstanding share capital as at the dates indicated:

	31 December 2007	31 December 2008	31 December 2009	As at the date of this Prospectus
Authorized share capital	1,000,000	1,000,000	1,000,000	1,300,000
Issued share capital in EUR	583,319.36	587,061.80	592,549.12	602,749.12
Issued share capital in number of shares	14,582,984	14,676,545	14,813,728	15,068,728

For an overview of the main changes in our issued share capital during the period covered by the historical financial information included in this Prospectus, reference is made to note 9 (Shareholders Equity) of the notes to the audited consolidated financial statements for the years 2009, 2008 and 2007.

#### Convertible loan notes

#### General

On 22 December 2009 we issued to funds associated with Forbion Capital Partners five-year unsecured and unsubordinated convertible loan notes (the "Loan Notes") for an aggregate amount of €5,000,000. The Loan Notes have a minimum denomination of €100,000, were issued at par and pay an annual coupon of 5%. The Loan Notes are due 31 December 2014. The Loan Notes contain a negative pledge undertaking from us.

#### Conversion

During the conversion period, which started 23 June 2010 and which ends on the final maturity date, 31 December 2014, the Loan Notes are convertible into our shares at an initial conversion price of €3.91.

The conversion price may be adjusted in the case of certain dilutive events such as (i) a share split or consolidation (ii) payment of stock dividend, (iii) and the issuance of shares or equity-linked securities at a substantial discount.

The conversion price adjustment in relation to the issue of shares at a substantial discount is applicable if we issue ordinary shares at an issue price per ordinary share that is less than 90% of the closing price on any trading day of the market price per ordinary share quoted at the close of business on Euronext Amsterdam on such trading day immediately preceding the pricing of the ordinary shares to be issued. In such an event the conversion price will be adjusted and the adjusted conversion price shall be determined as follows:

 $ACP = ((X + (Z \times c/P)) / (X + Z)) \times CP$ 

ACP = the conversion price as adjusted

X = the number of ordinary shares outstanding immediately prior to the

occurrence of such event

P = the arithmetic mean of the daily closing prices of the ordinary shares during the five trading day period immediately preceding the pricing of the shares to

be issued

Z = the number of ordinary shares to be issued

c = the issue price per share to be issued

CP = the conversion price immediately prior to the occurrence of such event

#### Call option

During the conversion period we have the option to call the conversion of the Loan Notes if our share price exceeds 150% of the then prevailing conversion price for a period of at least ten consecutive trading days.

Funds associated with Forbion Capital Partners were the initial holders of the tradable Loan Notes. The Loan Notes are not listed.

# **Depositary receipts for shares**

Out of the 15,068,728 currently issued shares, 624,400 are held by the Depositary in the context of the Share Incentive Plan. For the shares held by the Depositary, it has issued depositary receipts to the members of the Board of Management, members of Senior Management, certain of our employees and others. See also "Management and Employees – Share Incentive Plan".

#### Form and transfer of shares

All our shares are registered shares (aandelen op naam) and are eligible for inclusion in a collection deposit (verzameldepot) and/or giro deposit (girodepot) on the basis of the Securities Giro Act (Wet Giraal Effectenverkeer). The affiliated institutions (aangesloten instellingen), as defined in the Securities Giro Act, are responsible for the management of the collection deposit and Euroclear Netherlands, being the central institute (Centraal Instituut) for the purposes of the Securities Giro Act, will be responsible for the management of the giro deposit. The Articles of Association exclude the transfer of our shares out of a collective depot or a giro depot as set out in the Securities Giro Act.

#### Issue of shares and rights to subscribe for shares

Pursuant to the Articles of Association, the General Meeting of Shareholders is authorized to issue shares or grant rights to subscribe for shares, unless it has delegated this authority to another corporate body. Each resolution of the General Meeting of Shareholders to issue shares or grant rights to subscribe for shares, or to delegate this authority to another company body can only be adopted at the proposal of the Board of Management that has been approved by the Supervisory Board. The resolution of the General Meeting of Shareholders to delegate the authority to issue shares or grant rights to subscribe for shares cannot be revoked, unless determined otherwise at the time of delegation. No resolution of the General Meeting of Shareholders or the corporate body to which the authority to issue shares is delegated is required for an issue of shares pursuant to the exercise of a previously granted right to subscribe for shares.

Pursuant to a resolution taken by our General Meeting of Shareholders on 28 April 2010, the Board of Management has been granted the authority, subject to approval by the Supervisory Board, to issue shares or grant rights to subscribe for shares up to the amount of our authorized capital for a period that ends on 28 October 2011.

# **Pre-emptive rights**

Dutch law and the Articles of Association grant shareholders pre-emptive rights to subscribe on a pro rata basis for any issue of new shares or upon a grant of rights to subscribe for shares. Such pre-emptive rights do not apply, however, in respect of (i) shares issued for a non-cash contribution (ii) shares issued to our employees and (iii) shares issued to persons exercising a previously granted right to subscribe for shares.

Pursuant to the Articles of Association, the General Meeting of Shareholders is authorized to limit or exclude pre-emptive rights in relation to an issue of shares or grant rights to subscribe for shares, unless it has delegated this authority to another corporate body. Each resolution of the General Meeting of Shareholders to limit or exclude pre-emptive rights, or to delegate this authority to another company body can only be adopted at the proposal of the Board of Management that has been approved by the Supervisory Board. The resolution of the General Meeting of Shareholders to delegate the authority to limit or exclude pre-emptive rights cannot be revoked, unless determined otherwise at the time of delegation.

Pursuant to a resolution taken by our General Meeting of Shareholders on 28 April 2010, the Board of Management has been granted the authority, subject to approval by the Supervisory Board, to limit or exclude pre-emptive rights for a period that ends on 28 October 2011.

#### Acquisition of shares in our capital

We may not subscribe for our own shares on issue. 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 the 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 the 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, we may only acquire our own shares subject to a resolution of the Board of Management, 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 of 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.

Pursuant to a resolution taken by our General Meeting of Shareholders on 28 April 2010, the Board of Management is authorized for a period that ends on 28 October 2011 to acquire on the Company's behalf a maximum of 10% of our issued shares at a purchase price which shall not be less than the nominal value of our shares and shall not be higher than 10% above the average closing price of our shares during five consecutive trading days prior to the date of 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 under a scheme applicable to such employees. We may not vote on any shares held in our own capital and these shares will not be counted for voting quorum purposes.

# Reduction of share capital

Under the Articles of Association and subject to Dutch law, upon a proposal of the Board of Management, subject to the approval of the Supervisory Board, the General Meeting of Shareholders may resolve to reduce our issued and outstanding share capital by cancelling our shares, or by amending the 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.

The Board of Management 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 shares.

Under the Articles of Association, we may only make a distribution of dividends to our shareholders after adoption of our annual accounts demonstrating that such distribution is legally permitted. With the approval of the Supervisory Board, with due observance of applicable law, the Board of Management may declare an interim dividend on the shares.

The General Meeting of Shareholders may, at the proposal of the Board of Management, which proposal is subject to approval by the Supervisory Board, resolve that a distribution of dividends on the shares shall not be paid in whole or in part in cash, but in shares.

Each of our shares entitles its holder to equal ranking rights to dividends and other distributions.

Claims to dividends and other distributions not made within five years from the date that such dividends or distributions became payable, will lapse (*verjaren*) and any such amounts will be considered to have been forfeited to us.

# **General Meetings of Shareholders and voting rights**

The annual General Meeting of Shareholders shall be held within four 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 Board of Management 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 the Articles of Association, request that a General Meeting of Shareholders be convened. If such General Meeting of Shareholders has not been called within 14 days or is not held within one month following such request, the shareholders requesting such General Meeting of Shareholders are authorized to call such General Meeting of Shareholders themselves.

The notice of a General Meeting shall be published no later than the 42th day prior to the General Meeting. The notice shall be published on our website and remain directly and permanently accessible until the General Meeting of Shareholders. With due observance of the Dutch Civil Code, 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 or shares representing a value of at least €50 million according to the Daily Official List may submit proposals supported by reasons for the agenda. Provided we receive such proposals no later than the 60th day before the date of the General Meeting of Shareholders, we will have the proposals included in the notice for the General Meeting of Shareholders or, if necessary, in a supplemental notice.

Furthermore, 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 also be effected by means of a publication on our website.

Each of our shares entitles the holder thereof 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.

The Board of Management may determine that those entitled to attend, address and/or vote in a General Meeting of Shareholders, may do so by means of electronic communication, provided that such means of communication complies with certain requirements imposed by the Dutch Civil Code. The Board of Management may subject the use of the electronic

communication and the manner in which the requirements should be satisfied to conditions, which shall be stated in the notice of the General Meeting of Shareholders.

The Board of Management may determine in such convocation that any vote cast prior to the meeting by means of electronic communication, shall be deemed to be a vote cast in the meeting. Such a vote may not be cast prior to the record date, which record date shall be the 28th day before the General Meeting of Shareholders. A holder of shares who has cast his vote prior to the meeting by means of electronic communication, remains entitled to, whether or not represented by a holder of a written or electronically submitted proxy, participate in the General Meeting of Shareholders and to address such meeting. Once cast, an electronically cast vote cannot be revoked.

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 the Articles of Association and change of our corporate form

The General Meeting of Shareholders may resolve to amend the Articles of Association, subject to a proposal by the Board of Management, 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 the Articles of Association, subject to a proposal by the Board of Management, 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 Board of Management, which requires the approval of the Supervisory Board. In the event we are the acquiring company, the Board of Management 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 Board of Management 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 Board of Management, 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 the Articles of Association, and the members of the Board of Management will (unless otherwise determined by the General Meeting of Shareholders) become liquidators, acting under supervision of the Supervisory Board. During liquidation, the provisions of the Articles of Association will remain in force to the extent possible.

The balance remaining after settlement of debts shall be distributed to the holders of shares, in proportion to the aggregate nominal amount of their shares.

# **Dutch Corporate Governance Code**

On 9 December 2003, the Dutch Corporate Governance Committee, also known as the Tabaksblat Committee, released the Dutch Corporate Governance Code which was amended with effect from 1 January 2009 (the **"Code"**).

The Code contains principles and best practice provisions for management boards, supervisory boards, shareholders and general meetings of shareholders, financial reporting, auditors, disclosure, compliance and enforcement standards.

Companies having their corporate seat in the Netherlands and their shares admitted on a regulated market such as Euronext Amsterdam or on certain other stock exchanges are required to disclose in their annual reports whether or not they apply the provisions of the Code that are addressed to their management board or supervisory board and, if they do not apply, to explain the reasons why. The 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 Code.

We apply all of the relevant provisions of the Code with the following deviations which, together with the reasons for those deviations, are set out below. Although our deviations shall be disclosed in our annual reports, we shall not ask the General Meeting of Shareholders to explicitly approve such deviations.

#### Deviations from the Code

II.2.6 The supervisory board shall draw up regulations concerning ownership of and transactions in securities by management board members, other than securities issued by their 'own' company. The regulations shall be posted on the website. A management board member shall give periodic notice, but in any event at least once a quarter, of any changes in his holding of securities in Netherlands listed companies to the compliance officer or, if the company has not appointed a compliance officer, to the chairman of the supervisory board. A management board member who invests exclusively in listed investment funds or who has transferred the discretionary management of his securities portfolio to an independent third party by means of a written mandate agreement is exempted from compliance with this last provision.

We believe that the restrictions under Dutch securities law are sufficient to govern the ownership of and transactions in securities by members of the Board of Management. Implementing additional restrictions would potentially harm our ability to attract and ensure the continued services of the members of the Board of Management and we therefore believe that applying this best practice provision is not in our best interest.

II.2.10 If a variable remuneration component conditionally awarded in a previous financial year would, in the opinion of the supervisory board, produce an unfair result due to extraordinary circumstances during the period in which the predetermined performance criteria have been or should have been achieved, the supervisory board has the power to adjust the value downwards or upwards.

We believe that to be able to attract the best qualified candidates available for our Board of Management, we must be able to offer the best conditions available to us. We furthermore believe that by negotiating the discretion of the Supervisory Board proposed by this provision and the uncertainty entailed thereby would limit our abilities to attract these best qualified candidates.

II.2.11 The supervisory board may recover from the management board members any variable remuneration awarded on the basis of incorrect financial or other data (claw-back clause).

We believe that compliance with this provision would also limit our abilities to attract the best qualified candidates available for our Board of Management.

III.1.7 The supervisory board shall discuss at least once a year on its own, i.e. without the management board being present, its own functioning, the functioning of its committees and its individual members, and the conclusions that must be drawn on the basis thereof. The desired profile, composition and competence of the supervisory board shall also be discussed. Moreover, the supervisory board shall discuss at least once a year without the management board being present both the functioning of the management board as an organ of the company and the performance of its individual members, and the conclusions that must be drawn on the basis thereof. The report of the supervisory board shall state how the evaluation of the functioning of the supervisory board, the separate committees and the individual supervisory board members has been carried out.

The functioning of the individual members and that of the Supervisory Board as a whole has on a continuing basis been the topic of bi-lateral communications among members of the Supervisory Board. It has however not explicitly been on the agenda of any of the formal meetings of the Supervisory Board. The Supervisory Board is aiming to implement a system to ensure that an assessment of such functioning will be regularly performed and that the outcome thereof will be explicitly discussed in at least one of its meetings.

III.3.1 The supervisory board shall prepare a profile of its size and composition, taking account of the nature of the business, its activities and the desired expertise and background of the supervisory board members. The profile shall deal with the aspects of diversity in the composition of the supervisory board that are relevant to the company and shall state what specific objective is pursued by the board in relation to diversity. In so far as the existing situation differs from the intended situation, the supervisory board shall account for this in the report of the supervisory board and shall indicate how and within what period it expects to achieve this aim. The profile shall be made generally available and shall be posted on the company's website.

Following the Supervisory Board's review of its size and composition as part of an ongoing process, the Supervisory Board has recently been restructured. Taking the restructuring into account, the Supervisory Board shall review its profile and expects to be prepare an amended profile and post the same on our website in due course.

III.4.1 The chairman of the supervisory board shall ensure that:

[...]

f) the supervisory board elects a vice-chairman:

Currently, the Supervisory Board has no vice-chairman. Because of its recent restructuring the Supervisory Board expects to elect a vice-chairman from its midst in the near future.

III.4.3. The supervisory board shall be assisted by the company secretary. The company secretary shall ensure that correct procedures are followed and that the supervisory board acts in accordance with its statutory obligations and its obligations under the articles of association. He shall assist the chairman of the

supervisory board in the actual organization of the affairs of the supervisory board (information, agenda, evaluation, training program, etc.). The company secretary shall, either on the recommendation of the supervisory board or otherwise, be appointed and dismissed by the management board, after the approval of the supervisory board has been obtained.

No formal company secretary has been appointed due to our small size. However, a substantial proportion of the role has been delegated to our legal advisers, who provide external advice.

III.4.4 The vice-chairman of the supervisory board shall deputize for the chairman when the occasion arises. By way of addition to best practice provision III.1.7, the vice-chairman shall act as contact for individual supervisory board members and management board members concerning the functioning of the chairman of the supervisory board.

Currently, the Supervisory Board has no vice-chairman. Because of its recent restructuring the Supervisory Board expects to elect a vice-chairman from its midst in the near future.

III.5.4 The audit committee shall in any event focus on supervising the activities of the management board with respect to:

[...]

- c) compliance with recommendations and observations of internal and external auditors:
- d) the role and functioning of the internal audit function;

We feel that our financial reporting will be sufficiently monitored by our audit committee and will at this point not appoint an internal auditor.

III.5.6 The audit committee shall not be chaired by the chairman of the supervisory board or by a former member of the management board.

We consider the position of chairman of the Audit Committee to be of such importance that it should at all times be designated to the best qualified person available to us, even if such designation would not be in line with this best practice provision. Mr. Verdonck is currently chairman of both the Supervisory Board and the Audit Committee as we believe he is currently the best qualified person available to us.

III.6.5 The terms of reference of the supervisory board shall contain rules on dealing with conflicts of interest and potential conflicts of interest between management board members, supervisory board members and the external auditor on the one hand and the company on the other. The terms of reference shall also stipulate which transactions require the approval of the supervisory board. The company shall draw up regulations governing ownership of and transactions in securities by management or supervisory board members, other than securities issued by their 'own' company.

We believe that the restrictions under Dutch securities law are sufficient to govern the ownership of and transactions in securities of other companies by members of the Board of Management or by members of the Supervisory Board. Implementing additional restrictions would potentially harm our ability to attract and ensure the continued services of the members of the Board of Management and of the Supervisory Board and we therefore

believe that applying the final sentence of this best practice provision is not in our best interest.

III.7.1 A supervisory board member shall not be granted any shares and/or rights to shares by way of remuneration.

We granted shares and/or depositary receipts for shares to the chairman and the members of the Supervisory Board. We believe that this is international common practice and we may in the future be required to commit ourselves to grant options to attract and ensure the continued services of the best qualified persons for the Supervisory Board. We therefore believes that applying this best practice provision is not in its best interests.

IV.1.4 The policy of the company on additions to reserves and on dividends (the level and purpose of the addition to reserves, the amount of the dividend and the type of dividend) shall be dealt with and explained as a separate agenda item at the general meeting.

We are not permitted by law to pay dividends because we have no retained profits on account of our history of making losses. However in order to comply with this requirement in the future, we will table dividend and reserve policy as a separate item at a General Meeting of Shareholders in future.

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 company's 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 webcasting or telephone. After the meetings, the presentations shall be posted on the company's website.

Considering our size, it would create an excessive burden to provide facilities which enable shareholders to follow in real time the meetings and presentations referred to in the best practice provision. We will, however, ensure that presentations are posted on its website immediately after the meetings in question.

IV.3.4 Analysts meetings, presentations to institutional or other investors and direct discussions with the investors may not take place shortly before the publication of the regular financial information (quarterly, half-yearly or annual reports).

We maintain an active program of meetings with investors, which it considers to be in our best interests as well as our shareholders. From time to time these meetings may take place shortly before the publication of regular financial information but in such circumstances no price sensitive financial information is disclosed. Our substantial research and development activities mean that we have a history of making losses and we believe that presently the main driver of price sensitive information is the progress that we make on our programs, and that consequently financial information may be of less interest to investors.

IV.3.12 The company shall give shareholders and other persons entitled to vote the possibility of issuing voting proxies or voting instructions, respectively, to an independent third party prior to the general meeting.

We are small and do not believe it is appropriate at this time to appoint an independent third party to hold proxies. We do allow for shareholders to appoint their own independent third party proxies.

IV.3.13 The company shall formulate an outline policy on bilateral contacts with the shareholders and publish this policy on its website.

This is a new requirement, introduced only by the implementation of the currently prevailing Code. We have not historically felt the requirement for such a policy and therefore did not comply. The Supervisory Board and Board of Management will review this requirement at the earliest suitable opportunity.

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 at this point not appoint an internal auditor.

#### **Disclosure of information**

As a Dutch company listed on Euronext Amsterdam, we are 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 are required to make generally available interim management statements inter alia containing an overview of important transactions and their financial consequences in the period starting ten weeks after and ending six weeks before the first and second half of each financial year.

In addition we must make a document generally available to the public each year that contains or refers to the information we have made publicly available as described in the preceding paragraph.

Pursuant to the Financial Supervision Act we must make public, by means of a press release, certain 'inside information'. Inside information is knowledge of concrete information directly or indirectly relating to us or the trade in our shares or securities whose value partly depends on our shares which has not been made public and publication of which could significantly affect the trading price of our shares or securities whose value partly depends on our shares. Besides making this inside information public, we must also provide the AFM with this inside information at the time of publication and we must without delay publish the inside information on our website and keep it available on our website for at least one year.

# Obligations of shareholders to make a public offer

Pursuant to Chapter 5.5 of the Financial Supervision Act on takeover bids, a person who acquires at least 30% of our voting rights will be obliged to launch a public offer for all our outstanding shares. This obligation also applies to persons who, acting in concert, acquire at least 30% of our voting rights.

# Squeeze out proceedings

A person or company (alone or together with group companies) that holds at least 95% of the issued share capital for his own account can bring an action before the Enterprise Chamber of the Amsterdam Court of Appeal against the minority shareholders for the mandatory transfer of their shares to it. The price to be paid for the remaining securities will be determined by the Enterprise Chamber.

An offeror that has made a public bid and following such bid, holds at least 95% of our shares for his own account and represents at least 95% of the total voting rights attached to

our shares can bring an action before the Enterprise Chamber against the minority shareholders for the mandatory transfer of their shares to the offeror. This action should be instituted with three months after the end of the acceptance period under the public bid. The price to be paid for the remaining securities will be determined by the Enterprise Chamber, however starting point is, that in the event of a mandatory offer, the 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 if at least 90% of the shares have been acquired.

Within three months after the expiry of the acceptance period under a public offer and provided that the offeror has acquired at least 95% of the issued share capital for his own account and holds at least 95% of the voting rights, each minority shareholder can bring an action for the mandatory transfer of its shares before the Enterprise Chamber to the offeror. The price to be paid will be determined by the Enterprise Chamber. The starting point of the Enterprise Chamber for what is deemed to be a reasonable price is the same as set out in the second half of the previous paragraph.

# Notification of holdings of voting rights and capital interest

Pursuant to the Financial Supervision Act and the Decree on the Disclosure of Major Holdings and Capital Interests in Securities-Issuing Institutions (*Besluit melding zeggenschap en kapitaalbelang in uitgevende instellingen*), certain notification requirements apply to us as well as to holders of our shares.

Pursuant to the Financial Supervision Act, any person whose holding of voting rights and/or capital interest in us, directly or indirectly, reaches, exceeds or falls below the following thresholds: 5%, 10%,15%, 20%, 25%, 30%, 40%, 50%, 60%, 75% and 95% must notify the AFM without delay by means of a standard form or through the automated notification system of the AFM. We note that at the date of this Prospectus, a legislative proposal (Legislative Proposal 32 014) is pending which, if enacted without amendment, shall introduce an additional notification threshold of 3%. Legislative Proposal 32 014 also aims to introduce the obligation for persons that need to notify their holdings per the Financial Supervision Act to concurrently give the AFM notice whether they object to the strategy that a Dutch company that has securities which are admitted to trading on a regulated market shall need to publish on its website pursuant to Legislative Proposal 32 014, and of any subsequent changes in their position in relation to the company's strategy as notified to the AFM.

It is unclear if and when the above described proposed legislation will become effective. Once effective, the definitive amendment of the Financial Supervision Act may deviate from the above described proposals, due to amendments made during the legislative process.

We must notify the AFM without delay of any changes of 1% or more in our share capital and/or voting rights since the last notification we made to the AFM. Changes that amount to less then 1% must also be notified to the AFM but can be notified periodically.

The AFM keeps a public register of all such notifications. 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 the 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 the 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.

Members of our Board of Management and Supervisory Board must notify the AFM of their interest in our share capital and voting rights within two weeks of their appointment. Any subsequent change of their interest in our share capital and voting rights must be notified to the AFM without delay.

The following interests must be taken into account in determining the percentage of capital interest or voting rights: shares, depositary receipts or voting rights held (acquired and/or disposed of) (in)directly by any person (ii) shares, depositary receipts or voting rights held (acquired and/or disposed of) by a controlled undertaking of such person or by a third party for such person's account or by a third party with whom such person has concluded a voting agreement (including a discretionary power of attorney), and (iii) shares, 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). In addition, a right of pledge or usufruct on shares or depositary receipts must be added to the percentage of capital interest or voting rights if the pledge or usufructuary can obtain the right to vote on such shares and/or depositary receipts. 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.

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.

Non-compliance with these notification obligations is an economic offence and may lead to criminal prosecution. The AFM may impose administrative penalties or a cease-and-desist order under penalty for non-compliance. If criminal charges are pressed, it is no longer allowed to impose administrative penalties and vice versa. In addition, a civil court can impose measures against any person who fails to notify or incorrectly notifies the AFM of matters required to be correctly notified. A claim requiring that such measures be imposed may be instituted by us and/or one or more shareholders who alone or together with others represent(s) at least 5% of our issued and outstanding share capital.

The measures that the civil court may impose include:

• an order requiring the person violating the notification obligations under the Financial Supervision Act to make appropriate notification;

- suspension of voting rights in respect of such person's shares for a period of up to three years as determined by the court;
- voiding a resolution adopted by a general meeting of shareholders, if the court
  determines that the resolution would not have been adopted but for the exercise of the
  voting rights of the person who is obliged to notify, or suspension of a resolution until the
  court makes a decision about such voiding; and
- an order to the person violating the disclosure obligations under the Financial Supervision Act to refrain, during a period of up to five years as determined by the court, from acquiring the shares and/or voting rights in the shares.

#### Market abuse regime

The rules on preventing market abuse set out in the Financial Supervision Act are applicable to the members of our Board of Management and our Supervisory Board, and other insiders and persons performing or conducting transactions in our securities.

For the purpose of the Financial Supervision Act our insiders are (i) members of our Board of Management and our Supervisory Board, (ii) 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).

Our insiders 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. 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. Subject to certain criteria and circumstances, the notification by the insider may be postponed 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 Board of Management or Supervisory Board has notified a transaction to the AFM as described above under "Notification of holdings of voting rights and capital interests" such notification does suffice for the purposes described in this paragraph as well.

The AFM keeps a public register of all notifications made pursuant to the Financial Supervision Act. Non-compliance with the Dutch market abuse rules set out in this Chapter could constitute an economic offense and/or a crime (misdrijf) and could lead to the imposement of administrative fines by the AFM. The public prosecutor could press criminal charges resulting in fines or imprisonment. If criminal charges are pressed, it is no longer allowed to impose administrative penalties and vice versa.

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 Board of Management, our Supervisory Board and our employees. Further, we have drawn up a list of those persons working for us 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 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. However, claims with regard to mandatory public offers should be filed with the Enterprise Chamber of the Amsterdam Court of Appeal.

The AFM is the competent authority for approving all prospectuses published for admission of securities to trading on Euronext Amsterdam, except for prospectuses approved in other European Economic Area states that are used in the Netherlands in accordance with applicable passporting rules and the AFM supervisory powers with respect to publication of inside information by listed companies. In case of non-compliance the AFM may report this to the public prosecutor, who may continue the investigations.

The surveillance unit of Euronext Amsterdam continues to monitor and supervise all trading operations.

# **Private Placement**

### **Private Placement**

The Private Placement is conducted to strengthen our financial position and generate additional working capital to fund our operations.

The Private Placement consists of an offering of up to €16.3 million in New Shares. The New Shares shall be issued pursuant to an offering outside of the United States in "offshore transactions" within the meaning of, and pursuant to, Regulation S under the Securities Act by means of a private placement to certain institutional investors, other qualifying investors who subscribe for at least €50,000 per investor in various jurisdictions and to the members of the Board of Management.

The Private Placement shall be structured as an accelerated bookbuilt offering starting on 5 October 2010 immediately after the publication of this Prospectus and expected to close on 7 October 2010, subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances.

The Issue Price and the actual number of the New Shares issued pursuant to the Private Placement will be determined by us and the joint global coordinators of the Private Placement - Kempen & Co and Petercam Nederland - on the basis of the accelerated bookbuilding process and on the basis of the quoted share price as well as the demand in the Private Placement, taking into account market conditions, a qualitative assessment of demand for the New Shares and any other factors deemed appropriate.

The Issue Price, the actual number of New Shares issued pursuant to the Private Placement and the proceeds of the Private Placement shall be incorporated in a pricing statement which will be deposited with the AFM and published in a press release and on our website on or about 7 October 2010, subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances.

The arrangements we will enter into with the joint global coordinators in relation to the Private Placement provide that, upon the occurrence of certain events, such as the New Shares not being admitted to trading and listing on Euronext Amsterdam, the joint global coordinators have the right not to proceed with the closing of the Offering.

Funds managed by Gilde Healthcare Partners, Advent Venture Partners, Crédit Agricole and Forbion Capital Partners have committed to us to participate in the Private Placement for an amount of €1.5 million, €1 million, €750,000 and €500,000 respectively. The members of the Board of Management have expressed their intention to participate in the Private Placement.

We are not taking any action to permit a public offering of the New Shares in any jurisdiction. The statutory pre-emptive rights (*voorkeursrechten*) of the holders of our shares shall be excluded with respect to the Private Placement.

# **Dilution**

At the date of this Prospectus, the Company's authorized capital amounts to €1,300,000 divided into 32,500,000 shares with a nominal value of €0.04 each. At the date of this Prospectus, and consequently prior to the issue of any New Shares, the Company's issued and outstanding share capital amounts to €602,749.12 consisting of 15,068,728 shares with a nominal value of €0.04 each.

In the hypothesis that the Issue Price equals the closing price of our shares on 4 October 2010 - being €2.00 - and assuming we raise gross proceeds of €16.3 million in the Private Placement, the issued and outstanding share capital immediately following the issue of the New Shares shall amount to €928,749.12 consisting of 23,218,728 shares, resulting in an immediate dilution as a consequence of the Private Placement of 54% and amounting to €16.3 million. The actual dilution shall be dependent on the actual Issue Price as to be determined on the basis of the accelerated bookbuilding process and the amount raised in the Private Placement.

# **Listing of the New Shares**

We will apply for admission of the New Shares to listing and trading on Euronext Amsterdam. We expect that trading in the New Shares on Euronext Amsterdam will commence on or about 12 October 2010, subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances.

# Payment and settlement

Subject to acceleration or extension of the timetable of the Private Placement and barring unforeseen circumstances, payment and settlement of the New Shares which shall be issued pursuant to the Private Placement is expected to occur on or about 12 October 2010, which is also the expected date of issue of the New Shares. Delivery of the New Shares shall take place through the book-entry facilities of Euroclear Netherlands only, in accordance with its normal settlement procedures applicable to equity securities and against payment for the New Shares in immediately available funds.

The address of Euroclear Netherlands is:

Euroclear Netherlands (Nederlands Centraal Instituut voor Giraal Effectenverkeer B.V.)
Herengracht 459-469
1017 BS Amsterdam
The Netherlands

### Listing agent and paying agent

Kempen & Co acts a listing agent and as paying agent with respect to the admission to trading and listing the New Shares on Euronext Amsterdam.

# Ranking and dividends

Should the Board of Management propose in the future to grant a dividend, subject to approval of the Supervisory Board, the rights of holders of our shares, including the New Shares, will rank pari passu with each other.

# **Trading information**

Our shares are traded on Euronext Amsterdam under the following symbols:

ISIN Code: NL0000886968Common Code: 030386612

Symbol: "AMT"

# **Selling and Transfer Restrictions**

### **Notice to investors**

We have not taken any action to permit a public offering of the New Shares in any jurisdiction.

This Prospectus does not constitute an offer to sell, or a solicitation of an offer to buy, any of our shares or any other securities issued by us. This Prospectus will be sent for information purposes only and should not be copied or redistributed. If an investor receives a copy of this Prospectus, such investor may not treat the same as constituting an invitation or offer to the investor of any of our shares or any other securities issued by us.

If an investor receives a copy of this Prospectus or any other materials or advertisements referring to our shares or any other securities issued by us, the investor should not distribute or send the same, to any person, in or into any jurisdiction where to do so would or might contravene local securities laws or regulations. If an investor forwards this Prospectus or any other materials or advertisements referring to our shares or any other securities issued by us into any such territories (whether under a contractual or legal obligation or otherwise) such investor should draw the recipient's attention to the contents of this section.

# **Investors in the European Economic Area**

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), no New Shares have been or will be offered pursuant to the Private Placement to the public in the Relevant Member State, except that an offer to the public in that Relevant Member State of any New Shares may be made at any time under the following exemptions under the Prospectus Directive, if these exemptions have been implemented accordingly in that Relevant Member State:

- to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- to any legal entity which meets two or more of the following criteria (1) an average of at least 250 employees during the last financial year, (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in the relevant entity's last annual or consolidated accounts; or
- in any other circumstances which do not require the publication by us of a prospectus pursuant to article 3(2) of the Prospectus Directive;

provided that no such offer of New Shares shall result in a requirement for the publication of a prospectus pursuant to article 3 of the Prospectus Directive or any measure implementing the Prospectus Directive in a Relevant Member State and each person who initially acquires any New Shares or to whom any offer is made under the Private Placement will, unless under bullet point three above, be deemed to have represented, acknowledged and agreed that it is a "qualified investor", within the meaning of article 2(1)(e) of the Prospectus Directive as implemented in the respective member states.

For the purposes of this provision, the expression an "offer to the public" in relation to any New Shares in any Relevant Member State means the communication in any form and by any means of sufficient information the terms of the Private Placement and/or the New Shares be offered so as to enable an investor to decide to purchase or subscribe for New

Shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression Prospectus Directive includes any relevant implementing measure in each Relevant Member State.

### **Investors in the United States**

There will be no offering of the New Shares in the United States. The New Shares have not been and will not be registered under the Securities Act or under any securities laws of any state or other jurisdiction of the United States and may not be taken up, offered, sold, resold transferred, delivered or distributed, directly or indirectly, in or into or from the United States except pursuant to an applicable exemption from, or in a transaction not subject to, the registration requirements of the Securities Act and in compliance with the securities laws of any state or other jurisdiction of the United States. The New Shares to be issued pursuant to the Private Placement will be offered outside the United States in "offshore transactions" within the meaning of, and pursuant to Regulation S.

Each person to which the New Shares may be distributed, offered or sold outside the United States will be deemed by its subscription for, or purchase of, the New Shares to represent and agree, on its behalf and on behalf of any investor accounts for which it subscribes or purchases the New Shares, as the case may be, that:

- it acquires the New Shares from Amsterdam Molecular Therapeutics (AMT) Holding N.V. in an "offshore transaction" as defined in Regulation S under the Securities Act; and
- 2) the New Shares have not been offered to it by Amsterdam Molecular Therapeutics (AMT) Holding N.V. by means of any "directed selling efforts" as defined in Regulation S under the Securities Act.

Each subscriber or purchaser acknowledges that we will rely upon the truth and accuracy of the foregoing representations and agreements, and agrees that if any of the representations and agreements deemed to be made by such subscriber or purchaser by its subscription for, or purchase of, the New Shares, as the case may be, are no longer accurate, it shall promptly notify us. If such subscriber or purchaser is subscribing for, or purchasing, the New Shares as a fiduciary or agent for one or more investor accounts each subscriber or purchaser represents that it has sole investment discretion with respect to each such account and full power to make the foregoing representations and agreements on behalf of each such account.

### **Transfer restrictions**

Because of the following restrictions, purchasers are advised to consult legal counsel prior to making any offer, sales, resales, pledge or other transfer of the New Shares. The New Shares have not been registered under the US Securities Act and may not be offered or sold within the United States or to, or for the account or benefit of, US Persons, except to persons in offshore transactions in reliance on Regulation S or in the United States in private placement transactions not involving any public offering in reliance on the exemption from the registration requirements of Section 5 of the Securities Act provided by Section 4(2) under the Securities Act or another applicable exemption therefrom.

Each investor of the New Shares will be deemed to have represented and agreed as follows (terms used in this paragraph that are defined in Regulation S will have the corresponding meaning as they have in Regulation S):

- 1) The purchaser is (not a US Person and) is purchasing the New Shares in an offshore transaction pursuant to Regulation S;
- 2) The purchaser understands that the New Shares are being offered in a transaction not involving any offering in the United States within the meaning of the US Securities Act, that the New Shares have not been registered under the US Securities Act and that:
  - a) if in the future the investor decides to offer, resell, pledge or otherwise transfer any of the New Shares, such shares may be offered, resold, pledged or otherwise transferred only:
    - outside the United States in a transaction complying with the provisions of Regulation S;
    - ii. in the United States in private placement transactions not involving any public offering in reliance on the exemption from the registration requirements of Section 5 of the Securities Act provided by Section 4(2) under the Securities Act or another applicable exemption therefrom; or
    - iii. pursuant to an effective registration statement under the US Securities Act, in each case in accordance with any applicable securities laws of any state or other jurisdiction of the United States, and
  - b) the purchaser will, and each subsequent holder is required to, notify any subsequent purchaser of the New Shares from it of the resale restrictions referred to in (a) above.

# **Taxation**

This is a general summary and the tax consequences as described here may not apply to a holder of our shares. Any potential investor should consult his own tax adviser for more information about the tax consequences of acquiring, owning and disposing of our shares.

This taxation summary solely addresses the principal Netherlands tax consequences of the acquisition, the ownership and disposition of our shares. It does not discuss every aspect of taxation that may be relevant to a particular holder of our 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 Netherlands concepts, the meaning to be attributed to such terms and expressions shall therefore be the meaning to be attributed to the equivalent Netherlands concepts under Netherlands 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 laws of the Netherlands as they are in force and in effect on the date of this Prospectus. The laws upon which this summary is based are subject to change, possibly with retroactive effect. A change to such laws may invalidate the contents of this summary, which will not be updated to reflect any such changes.

# Taxes on income and capital gains

### Resident holders of shares

# General

The summary set out in this section "Taxes on income and capital gains - Resident holders of shares" only applies to a holder of shares who is a "Netherlands Individual" or a "Netherlands Corporate Entity."

For the purposes of this section you are a "Netherlands 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 Netherlands income tax purposes, or you have elected to be treated as a resident of the Netherlands for Netherlands income tax purposes;
- c. your shares and any benefits derived or deemed to be derived there from 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 Netherlands 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. Such person alone or, if he is an individual, together with his partner (partner, as defined in Article 1.2 of the Netherlands Income Tax Act 2001), if any, owns, directly or indirectly, 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 the ownership of 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. Such person's shares, profit participating certificates or rights to acquire shares or profit participating certificates in us have been acquired by him or are deemed to have been acquired by him under a non-recognition provision.
- 3. Such person's partner or any of his relatives by blood or by marriage in the direct line (including foster-children) or of those of his partner has a substantial interest (as described under 1. and 2. above) in us.

A person who is entitled to the benefits from shares or profit participating certificates (for instance a holder of a right of usufruct) is deemed to be a holder of shares or profit participating certificates, as the case may be, and his entitlement to benefits is considered a share or profit participating certificate, as the case may be.

If you are an individual and a holder of shares and if you satisfy test b., but do not satisfy test c. and/or test d., your Netherlands 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 "Taxes on income and capital gains – Non-resident holders of shares".

For the purposes of this section you are a "Netherlands Corporate Entity" if you satisfy the following tests:

- you are a corporate entity (including an association that is taxable as a corporate entity) that is subject to Netherlands corporation tax in respect of benefits derived from its shares:
- ii. you are resident, or deemed to be resident, in the Netherlands for Netherlands corporation tax purposes;
- iii. you are not an entity that, although in principle subject to Netherlands 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 the Netherlands Corporation Tax Act 1969 (Wet op de vennootschapsbelasting 1969).

If you are a corporate entity and a holder of shares and if you do not satisfy any one or more of these tests, with the exception of test ii, your Netherlands corporation tax position is not discussed in this Prospectus. If you are a corporate entity and a holder of shares that does not satisfy test ii, please refer to the section "Taxes on income and capital gains – Non-resident holders of shares."

Netherlands Individuals deriving profits from an enterprise

If you are a Netherlands Individual and if you derive or are deemed to derive any benefits from shares, including any capital gains realized on the disposal thereof, that are attributable to an enterprise from which you derive profits, whether as an entrepreneur (*ondernemer*) or

pursuant to a co-entitlement to the net value of an enterprise, other than as an entrepreneur or a shareholder, such benefits are generally subject to Netherlands income tax at progressive rates.

Netherlands Individuals deriving benefits from miscellaneous activities

If you are a Netherlands Individual and if you derive or are deemed to derive any benefits from shares, including any gain realized on the disposal thereof, that constitute benefits from miscellaneous activities (*resultaat uit overige werkzaamheden*), such benefits are generally subject to Netherlands income tax at progressive rates.

If you are a Netherlands Individual you may, inter alia, derive benefits from shares that are taxable as benefits from miscellaneous activities if your investment activities go beyond the activities of an active portfolio investor, for instance in the case of the use of insider knowledge (*voorkennis*) or comparable forms of special knowledge.

Netherlands Individuals deriving benefits from a lucrative interest

If you are a Netherlands Individual and if you derive any benefits from the holding, whether directly or indirectly, of (a combination of) shares, debt claims or other rights which form a "lucrative interest" (*lucratief belang*), such benefits are generally subject to Netherlands income tax at progressive rates.

A lucrative interest is an interest which the holder thereof has acquired under such circumstances that benefits arising from this lucrative interest are intended to be a remuneration for work or services performed by such holder (or a person related to such holder) in the Netherlands, whether within or outside an employment relationship, where such lucrative interest provides the holder thereof, economically, with certain benefits that have a relationship to the relevant work or services.

# Other Netherlands Individuals

If you are a Netherlands Individual and your situation has not been discussed before in this section "Taxes on income and capital gains – Resident holders of shares", benefits from your shares will be taxed as a benefit from savings and investments (*voordeel uit sparen en beleggen*). Such benefit is deemed to be four per cent. per annum of the average of your "yield basis" (*rendementsgrondslag*) at the beginning and at the end of the year, insofar as that average exceeds the "exempt net asset amount" (*heffingvrij vermogen*). The benefit is taxed at the rate of thirty per cent. The value of your shares forms part of your yield basis. Actual benefits derived from your shares, including any capital gains realized on the disposal thereof, are not as such subject to Netherlands income tax.

### Netherlands Corporate Entities

If you are a Netherlands Corporate Entity, any benefits derived or deemed to be derived by you from shares, including any capital gains realized on the disposal thereof, are generally subject to Netherlands corporation tax.

### Non-resident holders of shares

The summary set out in this section "Taxes on income and capital gains – Non-resident holders of shares" only applies to a holder of shares who is a Non-resident holder of shares.

For the purposes of this section, you are a "Non-resident holder of shares" if you satisfy the following tests:

- a. you are neither resident, nor deemed to be resident, in the Netherlands for purposes of Netherlands 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 Netherlands income tax purposes;
- b. your shares and any benefits derived or deemed to be derived there from 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 Netherlands Income Tax Act 2001, unless such interest forms part of the assets of an enterprise;
- d. if you are not an individual, no part of the benefits derived from your shares is exempt from Netherlands corporation tax under the participation exemption as laid down in the Netherlands Corporation Tax Act 1969; and
- e. you are not an entity that is resident in a Member State of the European Union and that is not subject to a tax on profits levied there.

See the section "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., d and e., your Netherlands 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 Netherlands 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 shares, including any capital gains realized on the disposal thereof, except if

- (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 "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.

# Dividend withholding tax

### General

We are generally required to withhold Dutch dividend tax at a rate of 15% from dividends distributed by us.

The concept "dividends distributed by us" as used in this section "Taxation" 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 Netherlands 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 Netherlands 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 Netherlands dividend withholding tax purposes, has been made or will be made; and
- partial repayment of capital, recognized as paid-in for Netherlands 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.

### Netherlands Individuals and Netherlands Corporate Entities

A Netherlands 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 Netherlands income tax purposes) and a Netherlands Corporate Entity generally can credit Netherlands dividend withholding tax against their Netherlands income tax or Netherlands corporation tax liability, as the case may be, and generally is entitled to a refund in the form of a negative assessment of Netherlands dividend withholding tax insofar as such tax, together with any other creditable domestic and/or foreign taxes, exceeds his aggregate Netherlands income tax or its aggregate Netherlands corporation tax liability, as the case may be, provided that, in the case of a Netherlands 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 Netherlands 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, Netherlands 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 there from 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 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 Netherlands income tax purposes, may be eligible for relief from Netherlands dividend withholding tax on the same conditions as an individual who is a Non-resident holder of shares, as discussed below.

See the section "Dividend withholding tax – General" for a description of the concept "dividends distributed by us."

See the section "Taxes on income and capital gains – Resident holders of shares" for a description of the terms Netherlands Individual and Netherlands 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 Netherlands 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 and that is resident in a Member State of the European Union is entitled to an exemption from dividend withholding tax, provided that the following tests are satisfied:

- 1. it takes one of the legal forms listed in the Annex to the EU Parent Subsidiary Directive (Directive 90/435/EEC, as amended), or a legal form designated by ministerial decree; and
- 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, and during that continuous one-year period would have been entitled to the participation exemption as meant in article 13 of the Netherlands Corporation Tax Act in respect of this shareholding, provided that such period ended after December 31, 2006; or
  - c. it is connected with us within the meaning of article 10a, paragraph 4, of the Netherlands Corporation Tax Act; or
  - d. an entity connected with it within the meaning of article 10a, paragraph 4, of the Netherlands Corporation Tax Act holds at the time the dividend is distributed by us, shares representing at least five per cent. of our nominal paid up capital; and

- 3. it is subject to the tax levied in its country of residence as meant in article 2, paragraph 1, letter c, of the EU Parent Subsidiary Directive (Directive 90/435/EEC, as amended) without the possibility of an option or of being exempt; and
- 4. it is not considered to be resident outside the Member States of the European Union under the terms of a double taxation treaty concluded with a third State.

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, or has owned, as the case may be, five per cent. of the voting rights in us.

See the section "Dividend withholding tax – Netherlands Individuals and Netherlands Corporate Entities" for a description of the term beneficial owner.

See the section "Taxes on income and capital gains – Non-resident holders of shares" for a description of the term Non-resident holder of shares.

### Gift and inheritance taxes

If you acquire shares as a gift (in form or in substance) or if you acquire or are deemed to acquire shares on the death of an individual, you will not be subject to Netherlands gift tax or to Netherlands inheritance tax, as the case may be, unless:

- the donor is, or the deceased was, resident or deemed to be resident in the Netherlands for purposes of gift or inheritance tax (as the case may be); or
- the shares are or were attributable to an enterprise or part of an enterprise that the
  donor or deceased carried on through a permanent establishment or a permanent
  representative in the Netherlands at the time of the gift or of the death of the deceased;
  or
- the donor made a gift of shares, then became a resident or deemed resident of the Netherlands, and died as a resident or deemed resident of the Netherlands within 180 days of the date of the gift.

# Other taxes and duties

No Netherlands registration tax, transfer tax, stamp duty or any other similar documentary tax or duty will be payable in the Netherlands in respect of or in connection with the subscription, issue, placement, allotment or delivery of the shares.

# **General Information**

### **Available information**

Annually, within four months of the end of our financial year, we are required to prepare and make generally available the annual financial statements consisting of (i) the audited annual accounts, (ii) the annual report, and, in addition thereto, (iii) responsibility statements of each member of the Board of Management and the Supervisory Board. Furthermore we are required to make generally available as soon as possible, but no later than two months after the end of the first half-year period of the financial year, our half-yearly financial statements consisting of (i) the half-yearly accounts, (ii) the half-yearly report, (iii) responsibility statements of each member of the Board of Management and the Supervisory Board and (iv) the auditor's report, if any. In addition we are required to make generally available interim management statements during each half-year period. The interim management statements will be made generally available in the period between ten weeks after the beginning and six weeks before the end of the relevant half-year period.

The financial information as described above will be made generally available by way of issuing a press release in which publication of the relevant financial information is announced with reference to our website where the relevant financial information will be available.

Copies of this Prospectus, our annual reports for the years 2009, 2008 and 2007, our unaudited condensed interim financial report for the six months ended 30 June 2010 and the Articles of Association may be obtained free of charge for a period of twelve months following the date of this Prospectus by sending a request in writing to us at our business address: Meibergdreef 61, 1105 BA Amsterdam Zuidoost, the Netherlands (tel.: +31 20 566 7394, e-mail: info@amtbiopharma.com), and are also available via www.amtbiopharma.com.

# **Corporate resolutions**

The Board of Management, with the approval of the Supervisory Board, is expected to resolve to issue the New Shares and to exclude the related pre-emptive rights of the existing holders of shares on or about 7 October 2010.

### Organizational structure

Amsterdam Molecular Therapeutics (AMT) Holding N.V. is a holding company of the following directly held subsidiaries.

Subsidiary	Country of incorporation	Percentage of ownership
Amsterdam Molecular Therapeutics (AMT) B.V.	The Netherlands	100%
Amsterdam Molecular Therapeutics (AMT) IP B.V.	The Netherlands	100%

# **Independent auditors**

Our audited consolidated financial statements as of and for each of the financial years in the three-year period ended 31 December 2009, 2008 and 2007, which are incorporated by reference in this Prospectus, have been audited by PricewaterhouseCoopers Accountants

N.V., independent auditors, as stated in its auditor' reports thereon, which are also, with the written consent of PricewaterhouseCoopers Accountants N.V., incorporated by reference in this Prospectus. Our unaudited consolidated interim financial report for the six months ended 30 June 2010, which is incorporated by reference in this Prospectus, has been reviewed by PricewaterhouseCoopers Accountants N.V., independent auditors, as stated in its review report thereon, which is also, with the written consent of PricewaterhouseCoopers Accountants N.V., incorporated by reference in this Prospectus. The auditor that signed the opinions is a member of the Royal Netherlands Institute of Chartered Accountants (Koninklijk Nederlands Instituut voor Registeraccountants).

# Independent patent and trade mark attorneys

At our request, Haseltine Lake LLP, European Patent and Trade Mark Attorneys, has undertaken to perform an independent review of our intellectual property portfolio based on information provided by us, and then to prepare the independent assessment of the IP portfolio which forms the report that, with the written consent of Haseltine Lake LLP, is included by means of Annex 1, in this Prospectus.

# Legal proceedings

Neither Amsterdam Molecular Therapeutics (AMT) Holding N.V. nor any of its subsidiaries is or has during the past 12 months been involved in any governmental, legal or arbitration proceedings which may have or have had significant effects on their financial position or profitability, nor are we aware of any such proceedings which are pending or threatened.

### **Material contracts**

Save as disclosed in "Description of Share Capital and Corporate Governance – Convertible loan notes", we have not entered into any contracts (not being contracts entered into in the ordinary course of business) within the two years immediately preceding the date of this Prospectus which are material, or at any other time and containing provisions under which we have an obligation or entitlement that is material as of the date of this Prospectus.

# **Definitions and Glossary**

The following definitions apply throughout this Prospectus, unless the context requires otherwise:

"AAV" adeno-associated viruses, i.e. a type of virus

which commonly infects humans without

causing disease

"AFM" the Netherlands Authority for the Financial

Markets (Stichting Autoriteit Financiële

Markten)

"AFSSAPS" the French regulatory authority for drug and

biological products (Agence Française de Sécurité Sanitaire des Produits de Santé)

"AGT" the enzyme alanine glyoxylate

aminotransferase, the presence of which enzyme in the liver is necessary to avoid the overproduction of oxalate (an end-product metabolite which has to be secreted by our

kidneys)

"AIP" or "acute intermittent porphyria" a monogenic metabolic orphan disease

characterized by insufficient function of PBGD in the liver, the patients of which disease lack a key enzyme that normally breaks down certain intermediate metabolites and generally suffer acute, severe attacks of abdominal pain, muscular weakness and a complex array of neuropathies (central nervous system malfunctions), including seizures, mental status changes, cortical blindness, coma,

and psychiatric symptoms

"AMC" the Academic Medical Center at the

University of Amsterdam

"Articles of Association" the articles of association (statuten) of the

Company as they read on the date of this

Prospectus

"ATMP" advanced medicinal therapy product

"Audit Committee" the audit committee of the Supervisory Board

"baculovirus" rod-shaped viruses that infect insects

"BGTD" biologics and genetic therapies directorate

"BLA" biologic license application "Board of Management" the management board (raad van bestuur) of the Company "CAT" committee for advanced therapy medicinal products "capsid" the protein shell of a virus particle surrounding its nucleic acid "cGMP" formal standards of a manufacturing facility's cleanliness, process, quality controls and documentation set out and periodically monitored by the main medicines control agencies to which a company has to conform in order to manufacture quantities of a medical product for clinical-phase testing "CHMP" committee for medicinal products for human use "Chylomicrons" particles which are the fat carrying responsible for pancreatitis in LPLD patients "CIMA" Center for Applied Medical Research (Centro de Investigación Médica Aplicada) "Company" Amsterdam Molecular Therapeutics (AMT) Holding N.V. "CTA" a clinical trial application "CVD" cardiovascular disease "Depositary" Stichting Participatieregeling AMT "dystrophin gene" the gene expressing the protein dystrophin "DMD" **Duchenne Muscular Dystrophy** "EMA" the European Medicines Agency which oversees the approval process for a new drug or device to be marketed "Euroclear Netherlands" Nederlands Centraal Instituut voor Giraal

"Euronext Amsterdam" NYSE Euronext in Amsterdam, the regulated market of Euronext Amsterdam N.V.

Effectenverkeer

B.V.

organization in the Netherlands

the

settlement

"Euronext" Euronext Amsterdam N.V.

"Financial Supervision Act" the Dutch Financial Supervision Act (Wet op het financieel toezicht) "FDA" the United States of America's Food and Administration, responsible overseeing the approval process for a new drug or device to be marketed "factor IX" essential blood clotting factor. deficiency of which prevents normal blood clotting "GCP" good clinical practice "GDNF" glial cell-derived neurotrophic factor, a protein that has been shown to promote the survival of various neurons "gene therapy" the use of genetic material to treat a disease. "General Meeting of Shareholders" any general meeting of the shareholders of the Company (algemene vergadering van aandeelhouders) "hemophilia B" a defect caused by an inherited deficiency of factor IX that prevents normal blood clotting in affected individuals that can result in bleeding diathesis, the most severe forms of which almost only affect male patients Health Canada the Canadian Federal department responsible for overseeing the approval process for a new drug or device to be marketed "Hyperlipoproteinemia type I" a rare metabolic orphan disease caused by inherited defects of the LPL gene and leading to dietary lipids, in particular triglycerides, to remain in the blood instead of being absorbed after each meal and metabolized, causing the blocking of small blood vessels, in particular of the pancreatic circulation, leading to the occurrence of pancreatitis "Hyperlipoproteinemia type V" a complex orphan metabolic disease, also known as mixed hypertriglyceridemia, that is characterized by both high blood serum triglycerides and hiah blood serum

kidneys

"hyperoxaluria"

cholesterol concentrations

Increased excretion of oxalate through the

"IFRS-EU" international financial reporting standards as

adopted by the European Commission for

use in the European Union

"IND" an investigational new drug

"IRB" institutional review board

"lentivirus" a genus of slow viruses of the Retroviridae

family, characterized by a long incubation period. lentiviruses can deliver a significant amount of genetic information into the DNA

of the host cell

"lipase" an enzyme that hydrolyzes fats

"lipid" fat

"lipoprotein" a conjugated protein that is a complex of

protein and lipid

"Loan Notes" the five-year unsecured and unsubordinated

convertible loan notes which have a minimum denomination of €100,000, pay an annual coupon of 5% and are due December 2014 issued by us on 22 December 2009

"LPL" Lipoprotein Lipase

"LPLD" Lipoprotein Lipase deficiency

"MAA" marketing authorization application

"named-patient sales program" a program which allows controlled, pre-

approval access to drugs in response to requests by physicians on behalf of specific, or "named", patients before those medicines are licensed in the patient's home country

"NDA" new drug application

"NDS" new drug submission

"New Shares" the new shares to be issued pursuant to the

Private Placement

"NIH" National Institutes of Health, a part of the

United States Department of Health and

**Human Services** 

"NOC" notice of compliance

"non-pathogenic" not capable of inducing disease

"orphan disease"

a rare disease that has such a low prevalence in a population that a doctor in a busy general practice would not expect to see more than one case a year. Rare diseases, including those of genetic origin, are life-threatening or chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them

"pancreatitis"

a severe and often lethal condition that requires intensive care, recurrent episodes of which condition destroy major parts of the pancreas eventually causing a form of diabetes that is difficult to treat

"PBGD"

porphobilinogen deaminase gene

"PD"

Parkinson's disease

"PH1" or "Primary hyperoxaluria type I"

a metabolic genetic disease characterized by a deficiency of the enzyme AGT, the lack of which enzyme (in presence or not functionality) causes the overproduction of oxalate by the liver to exceed the clearance ability of the kidneys and the remaining oxalate to precipitate as insoluble salts first in the kidneys and later in other organs

"PMPRB"

The Patented Medicine Prices Review Board

PoC

proof-of-concept

"porphobilogen deaminase"

a liver protein necessary for the production of

heme

"Prospectus"

this prospectus in accordance with article

5(3) of the Prospectus Directive

"Prospectus Directive"

directive 2003/71/EC

"QA"

quality assurance

"QC"

quality control

"R&D"

research and development

"Prospectus"

this Prospectus

"Remuneration and Nominating Committee"

the remuneration and nominating committee

of the Supervisory Board

"RNAi"

RNA interference

"Securities Act" the United States Securities Act of 1933, as

amended

"Securities Giro Act" Wet giraal effectenverkeer

"Share Incentive Plan" the share incentive plan of the Company

"Stock Option Plan" the stock option plan of the Company

"steatosis" accumulation of fat

"Supervisory Board" the supervisory board (raad van

commissarissen) of the Company

"T cell" a white blood cell involved in immune

reactions

"TOK" technisch ontwikkelingskrediet

"TOP" technisch ontwikkelingsproject

"TPD" therapeutic products directorate

"triglyceride" dietary fat

"vector" a viral protein particle containing a

therapeutic gene which can be used as a means of introducing such functional therapeutic genes into the appropriate target

tissue of a patient

# Annex - Independent Patent and Trade Mark Attorneys' Report

TRADE MARKS



DESIGNS

COPYRIGHT

The Directors Amsterdam Molecular Therapeutics (AMT) B.V. Meibergdreef 61 1105 BA Amsterdam Zuidoost Netherlands

30 September 2010

Dear Sirs

#### 1. Introduction

This Independent Patent and Trade Mark Attorneys' Report is given by David Brown, a partner with the firm of Haseltine Lake LLP, European Patent and Trade Mark Attorneys. Mr Brown has over twenty years' experience as a European and UK patent attorney, and became fully qualified (Chartered Patent Attorney, European Patent Attorney) in 1988. He has been a Registered Trade Mark Attorney since 1990 and a European Trade Mark Attorney since 1996. He joined Haseltine Lake LLP in 2001, and is experienced in all aspects of UK, European and International patent and trademark law in a wide range of technical fields related to pharmaceuticals and chemistry. Mr Brown has experience of providing Patent and Trade Mark Attorney's Reports for share issues on the London Stock Exchange.

Haseltine Lake LLP is one of the largest and longest established firm of Patent and Trade Mark Attorneys in Europe, having been in business since about 1850. Under the leadership of a professional Chief Executive, it has 31 registered attorneys and lawyers, 15 attorneys in training, as well over 50 other staff providing a range of services to clients including translation, renewal of intellectual property ("IP") rights, and on-line records and portfolio management services, and internal support services.

Haseltine Lake LLP has four offices in Europe, in London, Munich, The Hague and Bristol, as well as a representative office in Guangzhou, China.

Haseltine Lake LLP has not been involved in any way in the work to obtain the portfolio of IP rights set out in this Report. Haseltine Lake LLP has been engaged by Amsterdam Molecular Therapeutics (AMT) B.V.. ("the Company") specifically to review the IP portfolio on information provided by the Company, and then to prepare the independent assessment of the IP portfolio which forms this Report.

On information from the Company, the Company and Amsterdam Molecular Therapeutics (AMT) IP B.V. are wholly owned subsidiaries of Amsterdam Molecular Therapeutics (AMT) Holding N.V., and a primary purpose of Amsterdam Molecular Therapeutics (AMT) IP B.V. is to hold patent rights for the benefit of all three companies.

Haseltine Lake LLP has been assisted by Dr Mark Chadwick, Patent Counsel of the Company. This assistance comprises provision of a listing of the portfolio and a summary of the current procedural stage of each family of rights in the portfolio. On information from the Company, Dr Chadwick has held the position of Patent Counsel of the Company since November 2008. He holds a degree in Natural Sciences from the University of Cambridge and a Doctorate in Philosophy in Genetics from the University of East Anglia. Before joining the Company, Mr. Chadwick qualified as European Patent Attorney at J. A. Kemp and Co., where he spent 9 years. He then worked as European Patent Attorney for DSM, advising on their Food Specialties and White Biotechnology businesses.

On information from the Company, all registered IP rights currently owned by the Company or Amsterdam Molecular Therapeutics (AMT) IP B.V. or to which the Company holds a license have been disclosed to Haseltine Lake LLP and all such rights are listed in this Report.

Redcliff Quay 120 Redcliff Street Bristol BS1 6HU United Kingdom t: +44 (0)117 910 3200

www.haseltinelake.com www.haseltinelake.cn

Registration No. OC344156

### 1.1 Intellectual Property Rights

### (a) Patents

Patents are registered rights that protect inventions against unauthorised commercialisation. Patents are granted by national or regional Patent Offices if the invention satisfies particular legal requirements, primarily novelty and inventive step (non-obviousness). Patents grant the proprietor a monopoly right to prevent others from carrying out the invention claimed in the patent. The right, once granted, may be kept in force for a limited patent term (normally 20 years from the date of application for the patent) by payment of periodic (normally annual) renewal fees.

In certain circumstances, an effective patent term extension is available. In the case of pharmaceutical (including veterinary) products that have obtained regulatory approval in Europe, an extra 5.5 years of patent protection may be possible via the Supplementary Protection Certificate (SPC) system. This extension is designed to compensate the patentee for any undue delay in the regulatory approval process that the pharmaceutical product has been through. The SPC system requires a pharmaceutical regulatory delay – delays incurred before launching a functional food product do not qualify.

Patents are territorial rights that are effective within a given jurisdiction. For example, a UK national patent gives the proprietor the right to prevent unauthorised use of the invention in the UK, or to prevent importation of the invention in to the UK, but it does not have any effect in the USA or any other European country. Generally speaking, separate patents are required in each country where the invention will be commercially exploited.

An initial national patent application will usually serve as a so-called priority application for national applications to be filed in other countries and also for European patent applications or International (PCT) patent applications (see below).

A European patent application can cover one or more states that are party to the European Patent Convention. Such applications are searched and examined by the European Patent Office. The time taken at present from filing to grant can be considerable: it may take three to six years, or even longer, before a European patent is granted. After grant, to maintain rights in the desired states originally designated in the application, the European patent will need to be validated in those states. The European patent will then effectively be a bundle of national rights. It will be necessary to pay renewal fees in each national territory during the term of the patent, to maintain the patent rights.

If patent protection is desired in several territories, for example in Europe and beyond, there is the option to file an International (PCT) patent application. An International application will designate all countries party to the Patent Cooperation Treaty at the time of its filing (142 states as of 1 July 2010). This will generally cover most territories of commercial importance, including Europe, USA and Japan. An International application is normally filed within 12 months from the original priority-founding application. An authorised national or regional Patent Office will carry out a novelty search and a (non-binding) first stage examination procedure (leading to an International Preliminary Report on Patentability) on the International application. At about 30 months from filing, the International patent application must be brought into the national/regional phases in the territories of interest. Each national/regional application deriving from the International application will then be examined independently by the relevant national/regional patent office, and if the application meets the requirements of the law in the relevant territory a patent will be granted for that territory. Each national/regional application will have the same priority and filing dates as the International application.

### (b) Trade Marks

A trade mark registration gives its owner a monopoly right in the trade mark, or a confusingly similar mark, in respect of the goods or services for which the trade mark is registered, or similar goods or services. Trade mark rights may be kept in force indefinitely subject to the payment of renewal fees, usually at 10 year intervals. Generally speaking, a registered trade mark must be used by the proprietor in the territory of the registration to prevent it from becoming invalid.

### (c) Others

Other registered and unregistered forms of intellectual property can exist.

For example, utility models, registered designs and the SPCs mentioned above are all examples of registered intellectual property rights that can be obtained, in appropriate cases, in countries that provide for the grant of such rights in their national laws.

Certain international systems for streamlining the obtaining of such rights have been developed, although so far they are not as far developed as the international procedures for obtaining patents and for registering trade marks. Probably the best examples of international systems for obtaining registered rights outside the areas of patents and trade marks are in the international system for registering designs and the Community Registered Design, which is a single registered design enforceable in every country of the European Union.

On information form the Company, no such rights have been obtained by the Company.

Examples of unregistered intellectual property rights include copyright, unregistered design right, database right, unregistered trade mark rights deriving simply from use of a trade mark or other distinctive sign, the protective benefit of owning a domain name, and other protective rights such as those arising from duties to preserve confidentiality and secrecy of information received in confidence.

On information from the Company, such unregistered intellectual property rights exist and are held by the Company. However, this Patent and Trade Mark Attorneys' Report has excluded these rights from the scope of the review. Discussion of rights of confidentiality and secret information in a public document is clearly not appropriate. As far as other unregistered intellectual property rights are concerned, it is not recognized normal practice to review these in a Patent and Trade Mark Attorneys' Report of this type.

### 1.2 Details of Patent Applications and Granted Patents

The data set out below has been provided by the Company.

Haseltine Lake LLP has conducted sample checks to verify that the patent applications/granted patents are subsisting and have the status indicated below. On the basis of these checks, we have no reason to believe that the data provided by the Company is incorrect. As far as we are aware no relevant patent applications/granted patents exist to the Company other than those listed in this report. As far as we are aware, no adverse interests by third parties have been recorded against any of the listed patents or applications.

### 1.3 Details of Trade Mark Applications and Registrations

The data set out below has been provided by the Company.

Haseltine Lake LLP has conducted sample checks to verify that the trade mark applications and granted registrations are subsisting and have the status indicated below. On the basis of these checks, we have no reason to believe that the data provided by the Company is incorrect. As far as we are aware, no adverse interests by third parties have been recorded against any of the listed trade marks, other than those mentioned in Part 5 of this Report below.

# 2. The Company's Patent Policy

On information provided by the Company, the Company considers the acquiring and maintenance of intellectual property rights to be crucial to its business strategy and for the creation of value for the Company.

As mentioned above (Part 1 of this Report) in some cases Amsterdam Molecular Therapeutics (AMT) IP B.V. holds patent rights for the benefit of all three companies. On information from the Company, it is intended that in the future all patent rights will be held by Amsterdam Molecular Therapeutics (AMT) IP B.V. for the benefit of all the companies of the group, and the necessary intra-group transfers to give effect to this will be completed at the earliest convenient opportunity.

It is our opinion that the acquisition and maintenance of the IP portfolio of the Company has been pursued with skill and diligence, and all the evidence is that the Company does indeed place central importance on its intellectual property rights.

We record the following statement of IP Strategy that has been published by the Company, and confirm that in our opinion it is reasonable and, from the evidence we have seen, is being pursued as stated. We note that trade

mark filings have now been made (see Part 4 of this Report below). We also note that occasionally technology that is only the subject of pending patent applications is in-licensed (see, for example, "In-Licensed Family K" below):

"It is our policy to actively seek patent protection for our inventions and technologies and their uses. We analyze the results of our research and development activities regularly to identify patentable subject-matter and file new patent applications. In our dealings with our main collaborators we always ensure that we have rights in the intellectual property that results.

The Board of Management and our Senior Management have considerable individual and collective experience in the acquisition and management of intellectual property rights.

Whilst patents are the cornerstone of our proprietary protection, whether owned by us or in-licensed, in addition, we make use of trade secrets. 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. Glybera® is a registered trade mark in various jurisdictions including the EU. We will, in due course, make appropriate trade mark filings for our various other products.

We are reviewing the IP landscape for each of our products as part of the decision making process as to whether or not to continue development. If we identify third party patents that are reasonably likely to be valid and enforceable at that point, which may dominate our planned activities, we shall seek licenses at that time.

Our business is in a complex technical area due to the nature of the design of the products and their process of production and in this field there are many patents and patent applications, both published and unpublished. We only seek licenses to issued claims of third party patents where it is necessary to do so because the claims of such patents are reasonably likely to be valid and enforceable. We actively monitor the third party patent applications of which we are aware, but it is our policy not to seek licenses prior to any applicable patent application proceeding to grant when the granted claims become clear. When any of our products is in clinical development we review the intellectual property landscape for freedom to operate issues on an ongoing basis. If we identify third party patents that may cover our activities, which does occur from time to time in our field, we then conduct detailed validity analysis of any identified patents because the patent rights in question may be invalid and if so we would not approach the third party and seek a license to such rights. Where we conclude relevant patents are weak and in jurisdictions where it is possible to oppose the validity of such patents, it is our policy to do so. If we conclude that the patent is likely valid we then determine a potential licensing strategy and approach the third party in question."

### 3. Review and Analysis of The Company's Patent Portfolio

The patent families owned by or licensed to the Company or Amsterdam Molecular Therapeutics (AMT) IP B.V. are listed below.

Only patents and applications that have been published by the relevant Patent Offices are listed here. Patents and applications that are less than 18 months old, counted from the date of filing of the priority application, are held confidential within the relevant Patent Offices and are not available for public inspection.

We note that a clerical error was made in the papers by which the patent families 01 to 07 were filed and in subsequent assignment documentation. A company name "Amsterdam Molecular Therapeutics B.V." was used, instead of the correct company name "Amsterdam Molecular Therapeutics (AMT) B.V.". We expect that this error will be correctable in all countries. We have received assurances from the Company that, subject to local advice and procedures in the countries concerned, action is being or will be taken as soon as possible to correct the Patent Registers.

On information from the Company, in or about June 2007 the Company was incorporated under the name "Amsterdam Molecular Therapeutics (AMT) B.V." and the patent rights owned by the former company of that name were transferred to Amsterdam Molecular Therapeutics (AMT) IP B.V.. We have received assurances

from the Company that applications for recordal of that transfer on the Patent Registers will be made to the extent that they have not been made already.

On information from the Company, it is the Company's intention that all patent rights that it has applied for will be transferred to Amsterdam Molecular Therapeutics (AMT) IP B.V. to the extent that this has not been completed already.

### Concordance between Patent Family and Product

The following table has been provided by the Company, showing the concordance between each patent family and current products or plans of the Company.

Patent Family	Product	
01, A, B, G, L	GLYBERA®	
10, D	AMT-021	
J	AMT-060	
I	AMT-080	
D, E, H	AMT-090	
04, 05, 07, 08, C, F	General manufacturing (all products)	
02, 03, 06, 09, 11, K	possible future work	

### Families Owned or Co-Owned by the Company or Amsterdam Molecular Therapeutics (AMT) IP B.V.

### Family 01 – LPL Variant Therapeutics

This family is based on International (PCT) Patent Application No. PCT/CA00/00762 (Publication No. WO-A-01/00220). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the joint names of The University of British Columbia, Amsterdam Molecular Therapeutics B.V. and Academic Hospital at the University of Amsterdam. The European rights of Academic Hospital at the University of Amsterdam were later assigned to Amsterdam Molecular Therapeutics B.V. and have been recorded on the European Register of Patents. Therefore, the European rights are registered as co-owned by Amsterdam Molecular Therapeutics B.V. and The University of British Columbia. We have recommended that the actions to complete the legal transfer of these rights to the co-ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V, and The University of British Columbia are completed at an early stage. On information from the Company, the US rights are registered as owned by the inventors personally, and we have recommended that the rights of Amsterdam Molecular Therapeutics (AMT) IP B.V. in the US are secured and recorded on the US Register of Patents at an early stage. On information from the Company, the Japanese and Canadian rights are pending in the same names as on the original PCT application, and we recommend that the ownership of these rights is brought into line with the other family members before grant of any patents.

A European patent application (No. 99202048.7) was filed on 24 June 1999 and serves as priority founding application for the subsequently filed PCT application, filed on 23 June 2000.

The family relates to the use of a mutant form of the enzyme lipoprotein lipase (LPL) protein, and gene therapy vectors therefor, to treat a range of conditions responsive to LPL treatment, including pancreatitis. On information from the Company, this family protects aspects of the GLYBERA® product.

The current portfolio of patents and application is listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in June 2020, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in Austria No. 1200117

Patent in Belgium No. 1200117

Patent in Switzerland No. 1200117

Patent in Cyprus No. 1200117

Patent in Germany No. 50039880.3

Patent in Denmark No. 1200117

Patent in Spain No. 1200117

Patent in Finland No. 1200117

Patent in France No. 1200117

Patent in United Kingdom No. 1200117

Patent in Greece No. 1200117

Patent in Ireland No. 1200117

Patent in Italy No. 1200117

Patent in Luxembourg No. 1200117

Patent in Monaco No. 1200117

Patent in Netherlands No. 1200117

Patent in Portugal No. 1200117

Patent in Sweden No. 1200117

Patent Application in Canada No. 2,370,081

Patent Application in Japan No. 2001-505929

Patent Application in the United States No. 12/689236

On the basis of the cases that have proceeded to granted patents in at least one of the strict examining Patent Offices of the world, namely the European Patent Office, and no opposition was entered there against the patent, Haseltine Lake LLP expects the currently pending applications to proceed to granted patents in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

# <u>Family 02 – IL-10 Gene Transfer to Peripheral Mononuclear Cells</u>

This family is based on International (PCT) Patent Application No. PCT/NL03/00170 (Publication No. WO-A-03/074685). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Academisch Ziekenhuis bij de Universiteit van Amsterdam. On information from the Company, the European and US rights of Academisch Ziekenhuis bij de Universiteit van Amsterdam were later assigned to Amsterdam Molecular Therapeutics B.V. and this ownership was recorded on the European and US Registers of Patents. Therefore, these European and US rights are registered as solely owned by Amsterdam Molecular Therapeutics B.V.. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. are completed at an early stage.

A European patent application (No. 02075895.9) was filed on 7 March 2002 and serves as priority founding application for the subsequently filed PCT application, filed on 7 March 2003.

The family relates to the production of mononuclear cells overexpressing IL-10. On information from the Company, this family protects work that may be developed in the future.

The current portfolio of applications is listed below. Subject to grant in due course, patents on the applications have a potential expiry date in March 2023, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent Application in Europe No. 03715847 Patent Application in the United States No. 10/506881

We have reviewed public on-line file histories of the examination of these applications.

We find that at least some of the subject-matter of these applications has been considered patentable in principle in the US and European Patent Offices, which are strict examining Patent Offices, and that subject-matter is potentially of commercial significance. Therefore, we expect the currently pending applications to proceed to granted patents in due course.

# <u>Family 03 – Treatment of Non-alcoholic Steatotic Hepatitis</u>

This family is based on International (PCT) Patent Application No. PCT/NL2005/000446 (Publication No. WO-A-2005/123117). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the joint names of Academisch Ziekenhuis bij de Universiteit van Amsterdam and Amsterdam Molecular Therapeutics B.V.. On information from the Company, the rights of Academisch Ziekenhuis bij de Universiteit van Amsterdam were later assigned to Amsterdam Molecular Therapeutics B.V., and have been recorded on the relevant patent registers, in countries other than Australia, Canada, India, Japan and South Korea. Therefore, in those five countries the rights are still registered as jointly owned by Academisch Ziekenhuis bij de Universiteit van Amsterdam and Amsterdam Molecular Therapeutics B.V., whereas in the other countries listed below they are registered as owned solely by Amsterdam Molecular Therapeutics B.V.. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. are completed at an early stage.

A US patent application (No. 60/580903) was filed on 21 June 2004 and serves as priority founding application for the subsequently filed PCT application, filed on 20 June 2005.

The family relates to the use of LPL to treat non-alcoholic steatotic hepatitis (NASH). On information from the Company, this family protects work that may be developed in the future.

The current portfolio of patents and application is listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in June 2025, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in Austria No. 1761273

Patent in Belgium No. 1761273

Patent in Bulgaria No. 1761273

Patent in Switzerland No. 1761273

Patent in Cyprus No. 1761273

Patent in Czech No. 1761273

Patent in Germany No. 1761273

Patent in Denmark No. 1761273

Patent in Estonia No. 1761273

Patent in Spain No. 1761273

Patent in Finland No. 1761273

Patent in France No. 1761273

Patent in United Kingdom No. 1761273

Patent in Greece No. 1761273

Patent in Hungary No. 1761273

Patent in Ireland No. 1761273

Patent in Iceland No. 1761273

Patent in Italy No. 1761273

Patent in Lithuania No. 1761273

Patent in Luxembourg No. 1761273

Patent in Monaco No. 1761273

Patent in Netherlands No. 1761273

Patent in Poland No. 1761273

Patent in Portugal No. 1761273

Patent in Romania No. 1761273

Patent in Sweden No. 1761273

Patent in Slovenia No. 1761273

Patent in Slovakia No. 1761273

Patent in Turkey No. 1761273

Patent Application in Australia No. 2005253897

Patent Application in Canada No. 2,568,643

Patent Application in China No. CN 1972709 A

Patent Application in India No. 7309/DELNP/2006

Patent Application in Japan No. 2008-503569

Patent Application in South Korea No. 10-2006-7027008

Patent Application in the United States No. 11/570917

On the basis of the cases that have proceeded to granted patents in at least one of the strict examining Patent Offices of the world, namely the European Patent Office, and no opposition was entered there against the patent, Haseltine Lake LLP expects the currently pending applications to proceed to granted patents in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

### Family 04 – Improved AAV Vectors Produced in Insect Cells

This family is based on International (PCT) Patent Application No. PCT/NL2006/050262 (Publication No. WO-A-2007/046703). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Amsterdam Molecular Therapeutics B.V.. On information from the Company, no change of ownership has been registered. Therefore, the rights are registered as solely owned by Amsterdam Molecular Therapeutics B.V. and this is recorded on each relevant patent register. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. are completed at an early stage.

A PCT patent application (No. NL2005/050018) was filed on 20 October 2005 and serves as priority founding application for the subsequently filed PCT application, filed on 19 October 2006.

The family relates to the production of AAV vectors in insect cells. On information from the Company, this family protects aspects of the Company's general manufacturing platform, relevant or potentially relevant to all products.

The current portfolio of applications is listed below. Subject to grant in due course, patents on the applications have a potential expiry date in October 2026, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent Application in Australia No. 2006304997

Patent Application in Hong Kong No. 08111236.3

Patent Application in Canada No. 2,622,233

Patent Application in China No. 200680038430.6

Patent Application in Europe No. 06812721.6

Patent Application in India No. 2923/DELNP/2008

Patent Application in Japan No. 2009-512436

Patent Application in the United States No. 12/091022

We have reviewed public on-line file histories of the examination of these applications, including the International Preliminary Report on Patentability drawn up for the PCT application.

We find that at least some of the subject-matter of these applications has been considered novel in principle, but an objection has been raised in the European Patent Office that the claims are broader than the data in the application would support. This type of objection is common in biotechnology cases, but may be answered, in appropriate cases, by showing that the data in the application present the reader with the plausible expectation that the invention would indeed work across the full scope of the claims. Therefore, at this stage we expect that at least a portion of the currently pending claims can proceed to granted patents in due course. The extent to which the full scope of the current claims will be granted will depend on the skill of the Company's Patent

Counsel and any outside patent attorneys engaged to work on the case, in convincing the Examiners who raise such an objection that the reader has the plausible expectation that the invention will work across the full scope of the claims.

<u>Family 05 – Vectors With Modified Initiation Codon for the Translation of AAV-REP78 Useful for Production of AAV in Insect Cells</u>

This family is based on International (PCT) Patent Application No. PCT/NL2007/050298 (Publication No. WO-A-2007/148971). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Amsterdam Molecular Therapeutics B.V.. On information from the Company, no change of ownership has been registered. Therefore, the rights are registered as solely owned by Amsterdam Molecular Therapeutics B.V. and this is recorded on each relevant patent register. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. are completed at an early stage.

A US patent application (No. 60/815262) and European patent application (No. 06115804.4) were filed on 21 June 2006 and serve as priority founding applications for the subsequently filed PCT application, filed on 20 June 2007.

The family relates to nucleic acids for the production of recombinant AAV vectors in insect cells. On information from the Company, this family protects aspects of the Company's general manufacturing platform, relevant or potentially relevant to all products

The current portfolio of applications is listed below. Subject to grant in due course, patents on the applications have a potential expiry date in June 2027, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent Application in Australia No. 2007261806

Patent Application in Hong Kong No. 1127083A

Patent Application in Canada No. 2,655,957

Patent Application in China No. CN 101506369 A

Patent Application in Europe No. 07747521.8

Patent Application in Israel No. 196091

Patent Application in India No. 99/CHENP/2009

Patent Application in Japan No. 2009-540823

Patent Application in South Korea No. 2008-7031187

Patent Application in Russian Federation No. 2009101766

Patent Application in the United States No. 12/306239

We have reviewed public on-line file histories of the examination of these applications, including the International Preliminary Report on Patentability drawn up for the PCT application.

We find that at least some of the subject-matter of these applications has been considered novel in principle, but an objection has been raised in the European Patent Office that the novel claims lack an inventive step. This type of objection is common in biotechnology cases, but may be answered, in appropriate cases, by showing that there were circumstances that would have prevented a person of ordinary skill in the art from going obviously to the invention with a reasonable advance expectation of achieving the advantages which the invention provides, merely by reviewing the prior publications. The extent to which the Examiners who raise this objection can be persuaded that the said person of ordinary skill in the art would not have gone obviously to the invention will depend on the skill of the Company's Patent Counsel and any outside patent attorneys engaged to work on the case. Therefore, it is not possible at this stage to give a definitive opinion on the likelihood of success.

# <u>Family 06 – Use of AAV Replication Machinery for Improved Protein Production</u>

This family is based on International (PCT) Patent Application No. PCT/NL2008/050613 (Publication No. WO-A-2009/038462). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Amsterdam Molecular Therapeutics B.V.. On information from the Company, no change of ownership has been registered apart from in relation to the US application

which, as mentioned below, is owned by Amsterdam Molecular Therapeutics (AMT) IP B.V. Therefore, the rights are registered as solely owned by Amsterdam Molecular Therapeutics B.V (or, in the US, Amsterdam Molecular Therapeutics (AMT) B.V ) and this is recorded on each relevant patent register. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. in all countries are completed at an early stage.

A US patent application (No. 60/973517) and European patent application (No. 07075817.2) were filed on 19 September 2007 and serve as priority founding applications for the subsequently filed PCT application, filed on 18 September 2008.

The family relates to a method for enhancing the production of a gene expression product in a cell using AAV replication machinery. On information from the Company, this family protects work that may be developed in the future.

The current portfolio of applications is listed below. Subject to grant in due course, patents on the applications have a potential expiry date in September 2028, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent Application in Europe No. 08831795.3 Patent Application in Japan No. (not available) Patent Application in the United States No. 12/679144

We have reviewed public on-line file histories of the examination of these applications, including the International Preliminary Report on Patentability drawn up for the PCT application.

We find that the subject-matter of these applications has been considered novel in principle, but an objection has been raised in the European Patent Office that the claims lack an inventive step. This type of objection is common in biotechnology cases, but may be answered, in appropriate cases, by showing that there were circumstances that would have prevented a person of ordinary skill in the art from going obviously to the invention with a reasonable advance expectation of achieving the advantages which the invention provides, merely by reviewing the prior publications. The extent to which the Examiners who raise this objection can be persuaded that the said person of ordinary skill in the art would not have gone obviously to the invention will depend on the skill of the Company's Patent Counsel and any outside patent attorneys engaged to work on the case. Therefore, it is not possible at this stage to give a definitive opinion on the likelihood of success.

# Family 07 – Baculoviral Vectors Comprising Repeated Coding Sequences with Differential Codon Bases

This family is based on International (PCT) Patent Application No. PCT/NL2008/050512 (Publication No. WO-A-2009/014445). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Amsterdam Molecular Therapeutics B.V.. On information from the Company, no change of ownership has been registered. Therefore, the rights are registered as solely owned by Amsterdam Molecular Therapeutics B.V. and this is recorded on each relevant patent register. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. are completed at an early stage.

A US patent application (No. 60/952081) and European patent application (No. 07113257.5) were filed on 26 July 2007 and serve as priority founding applications for the subsequently filed PCT application, filed on 25 July 2008.

The family relates to the production of proteins in insect cells using repeated coding sequences in baculoviral vectors. On information from the Company, this family protects aspects of the Company's general manufacturing platform, relevant or potentially relevant to all products.

The current portfolio of applications is listed below. Subject to grant in due course, patents on the applications have a potential expiry date in July 2028, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent Application in Australia No. 2008279883 Patent Application in Brazil No. PI 0814459-1 Patent Application in Canada No. 2,694,406

Patent Application in China No. 200880108079.2

Patent Application in Eurasian Patent Organisation No. 201070184

Patent Application in Europe No. 08779058.0

Patent Application in Israel No. 203535

Patent Application in India No. 721/CHENP/2010

Patent Application in Japan No. 2010-518140

Patent Application in South Korea No. 2010-7003963

Patent Application in Mexico No. MX/a/2010/000944

Patent Application in New Zealand No. 582881

Patent Application in the United States No. 12/670780

Patent Application in South Africa No. 2010/00561

We have reviewed public on-line file histories of the examination of these applications, including the International Preliminary Report on Patentability drawn up for the PCT application.

We find that the subject-matter of these applications has been considered to lack novelty and an inventive step, but only because the claims as presently worded are deemed not to be close enough to the priority founding application. It is our opinion that if the claims would be amended into conformity with the priority founding application the application would be allowable in principle and we could envisage patents being granted.

# <u>Family 08 – Optimisation of Expression of Parvoviral REP and CAP Proteins in Insect Cells</u>

This family is based on International (PCT) Patent Application No. PCT/NL2009/050076 (Publication No. WO-A-2009/104964). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Amsterdam Molecular Therapeutics B.V., which name was corrected in the international phase to Amsterdam Molecular Therapeutics (AMT) B.V.. On information from the Company, there has been no change of ownership. Therefore, the rights are solely owned by Amsterdam Molecular Therapeutics (AMT) B.V. and this is recorded on each relevant patent register. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. are completed at an early stage.

A US patent application (No. 61/029673) and European patent application (No. 08151634.6) were filed on 19 February 2008 and serve as priority founding applications for the subsequently filed PCT application, filed on 19 February 2009.

The family relates to improving the production of recombinant parvoviral virions in insect cells. On information from the Company, this family protects aspects of the Company's general manufacturing platform, relevant or potentially relevant to all products

The current portfolio of applications is listed below. Subject to grant in due course, patents on the applications have a potential expiry date in February 2029, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent Application in Australia No. (not yet available)

Patent Application in Canada No. (not yet available)

Patent Application in China No. (not yet available)

Patent Application in Eurasian Patent Organisation No. (not yet available)

Patent Application in Europe No. (not yet available)

Patent Application in Israel No. (not yet available)

Patent Application in India No. (not yet available)

Patent Application in Japan No. (not yet available)

Patent Application in the United States No. (not yet available)

We have reviewed public on-line file history of the searching of this international application.

While the applications are at an early stage, we note that at least some of the subject-matter of these applications has been considered patentable in principle in the European Patent Office (acting as International Searching Authority), which is a strict examining Patent Office, and that subject-matter is potentially of commercial

significance. Therefore, we expect that at least part of the currently claimed subject-matter of the pending applications to proceed to granted patents in due course.

### <u>Family 09 – Parvoviral Capsid with Incorporated Gly-Ala Repeat Region</u>

This family is based on International (PCT) Patent Application No. PCT/NL2009/050352 (Publication No. WO-A-2009/154452). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Amsterdam Molecular Therapeutics B.V.. Therefore, the rights are solely owned by Amsterdam Molecular Therapeutics B.V. We have recommended that the actions to complete the legal transfer of these rights to the sole ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. are completed at an early stage.

A European patent application (No. 08158418.7) and a US patent application (No. 61/073295) were both filed on 17 June 2008 and serve as priority founding applications for the subsequently filed PCT application, filed on 17 June 2009.

The family relates to a parvoviral virion for use in gene therapy. On information from the Company, this family protects work that may be developed in the future.

This family is too young to have entered its national and regional phases yet. Subject to grant in due course, patents on the application have a potential expiry date in June 2029, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval

We have reviewed the public on-line file history of the searching of this international application.

We find that potentially close prior art has been cited against the application. Therefore, it is not possible at this stage to offer any expectation that the currently pending claims will proceed to granted patents in due course. The extent to which this outcome may be achieved will depend on the skill of the Company's Patent Counsel and any outside patent attorneys engaged to work on the case, in finding in the application evidence of a patentable advance in view of the prior art and then presenting amended claims for the Patent Office Examiners to review.

# Family 10 - Porphobilinogen Deaminase Gene Therapy

This family is based on International (PCT) Patent Application No. PCT/NL2009/050584 (Publication No. WO-A-2010/036118). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the joint names of Amsterdam Molecular Therapeutics (AMT) B.V. and Proyecto de Biomedicina Cima S.L. Therefore, the rights are jointly owned by Amsterdam Molecular Therapeutics (AMT) B.V and Proyecto de Biomedicina Cima S.L. We have recommended that the actions to complete the legal transfer of these rights to the co-ownership of Amsterdam Molecular Therapeutics (AMT) IP B.V. and Proyecto de Biomedicina Cima S.L. are completed at an early stage.

A European patent application (No. 08165393.3) and a US patent application (No. 61/100881) were both filed on 29 September 2008 and serve as priority founding applications for the subsequently filed PCT application, filed on 29 September 2009.

The family relates to porphobilinogen deaminase gene therapy, that is gene therapy for treating the inherited condition acute intermittent porphyria (AIP). On information from the Company, this family protects aspects of the AMT-021 program.

This family is too young to have entered its national and regional phases yet. Subject to grant in due course, patents on the application have a potential expiry date in September 2029, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

We have reviewed the public on-line file history of the searching of this international application.

We find that potentially close prior art has been cited against the application. Therefore, it is not possible at this stage to offer any expectation that the currently pending claims will proceed to granted patents in due course.

The extent to which this outcome may be achieved will depend on the skill of the Company's Patent Counsel and any outside patent attorneys engaged to work on the case, in finding in the application evidence of a patentable advance in view of the prior art and then presenting amended claims for the Patent Office Examiners to review.

### Family 11 – Alanine-Glyoxylate Aminotransferase Therapeutics

This family is based on International (PCT) Patent Application No. PCT/NL2010/050044 (Publication No. WO-A-2010/087709). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the sole name of Amsterdam Molecular Therapeutics (AMT) IP B.V. Therefore, the rights are solely owned by Amsterdam Molecular Therapeutics (AMT) IP B.V.

A European patent application (No. 09151795.3) was filed on 30 January 2009 and serves as priority founding application for the subsequently filed PCT application, filed on 1 February 2010.

The family relates to alanine-glyoxylate aminotransferase therapeutics. On information from the Company, this family protects work that may be developed in the future.

This family is too young to have entered its national and regional phases yet. Subject to grant in due course, patents on the application have a potential expiry date in February 2030, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval

We have reviewed the public on-line file history of the searching of this international application.

We find that no close prior art has been cited against the application. Provided that this situation is maintained in the national and regional phases, we expect the currently pending claims to proceed to granted patents in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

# Families In-Licensed by the Company

# General Note

We have not reviewed the license agreements for the preparation of this Report. The factual information concerning the existence, structure and extent of the license is as provided by the Company.

As previously mentioned (section 1.2 above), we have conducted sample checks on the patents and patent applications identified below and find that all the checks correspond with the information provided by the Company. We therefore have no reason to doubt the information that has been provided.

We have received assurances from the Company that the license documents are being checked for the same clerical error relating to the Company's name (namely, omission of "(AMT)"), and that appropriate correction agreements will be concluded as soon as possible to the extent that the error has occurred.

### In-Licensed Family A – Recombinant Viruses, Preparation and Use Thereof in Gene Therapy

This family is based on International (PCT) Patent Application No. PCT/FR95/00669 (Publication No. WO-A-95/33840). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the name of Rhone-Poulenc Rorer SA. On information from the Company, the rights are now co-owned by The University of British Columbia and Aventis Pharma S.A.. A license to use the technology has been obtained.

A French patent application (No. 9406759) was filed on 2 June 1994 and serves as priority founding application for the subsequently filed PCT application, filed on 22 May 1995.

The family relates to the use of a range of defective recombinant viruses encoding all or part of LPL or a derivative thereof. On information from the Company, this family protects aspects of the GLYBERA® product.

On information from the Company, the licensed portfolio of patents and applications at the last review was at least the rights listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in May 2015, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in European countries\* No. 763117
Patent Application in Canada No. 2,190,394
Patent in the United States No. 6,814,962
Patent Application in Australia No. 9526205
Patent Application in Finland No. 9604784
Patent Application in Japan No. 10500859
Patent in Mexico No. (not available)
Patent in South Africa No. ZA9504386
Patent Application in Israel No. 113987
Patent in France No. 2720756

\* the European Patent Register indicates that this patent is in force in the following countries: Belgium, Germany, France, United Kingdom, Switzerland, Luxembourg, Netherlands.

On the basis of the cases that have proceeded to granted patents in strict examining Patent Offices of the world, Haseltine Lake LLP expects the currently pending applications to proceed to granted patents in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

<u>In-Licensed Family B – Adeno-Associated Virus Serotype 1 Nucleic Acid Sequences, Vectors and Host Cells</u> <u>Containing Same</u>

This family is based on International (PCT) Patent Application No. PCT/US99/25694 (Publication No. WO-A-00/28061). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the name of The Trustees of the University of Pennsylvania. On information from the Company, the rights are still owned by The Trustees of the University of Pennsylvania. A license to use the technology has been obtained.

A US patent application (No. 60/107114) was filed on 5 November 1998 and serves as priority founding application for the subsequently filed PCT application, filed on 2 November 1999.

The family relates to recombinant vectors, e.g. viruses, for use in gene delivery. On information from the Company, this family protects aspects of the GLYBERA® product.

On information from the Company, the licensed portfolio of patents and applications at the last review was at least the rights listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in November 2019, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in European countries No. 1127150
Patent Application in Canada No. 2,349,838
Patent in the United States No. 6,759,237
Patent in the United States No. 7,105,345
Patent in the United States No. 7,186,552
Patent Application in the United States No. 2006/0204479
Patent in Australia No. 768729
Patent Application in Australia No. 2004201463
Patent Application in Japan No. 2002529098

On the basis of the cases that have proceeded to granted patents in strict examining Patent Offices of the world, Haseltine Lake LLP expects the currently pending applications to proceed to granted patents in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

### *In-Licensed Family C – Production of Adeno-Associated Virus in Insect Cells*

This family is based on International (PCT) Patent Application No. PCT/US02/35829 (Publication No. WO-A-03/042361). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the name of Government of the United States of America, Department of Health and Human Services. On information from the Company, the rights are still owned by Government of the United States of America, Department of Health and Human Services. A license to use the technology has been obtained.

US patent applications (Nos. 09/986618 and 10/216870) were filed on 9 November 2001 and 13 August 2002 and serve as priority founding applications for the subsequently filed PCT application, filed on 8 November 2002.

The family relates to the production of adeno-associated viruses in insect cells. On information from the Company, this family protects aspects of the Company's general manufacturing platform, relevant or potentially relevant to all products.

On information from the Company, the licensed portfolio of patents and applications at the last review was at least the rights listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in November 2022, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in European countries No. 1572893 Patent Application in Canada No. 2,467,959 Patent in the United States No. 6,723,551 Patent in the United States No. 7,271,002 Patent Application in Australia No. 2002360355

On the basis of the cases that have proceeded to granted patents in strict examining Patent Offices of the world, Haseltine Lake LLP expects the currently pending applications to proceed to granted patents in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

# <u>In-Licensed Family D – AAV5 Vector and Uses Thereof</u>

This family is based on International (PCT) Patent Application No. PCT/US99/11958 (Publication No. WO-A-99/61601). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the name of Government of the United States of America, Department of Health and Human Services. On information from the Company, the rights are still owned by Government of the United States of America, Department of Health and Human Services. A license to use the technology has been obtained.

A US patent application (No. 60/087029) was filed on 28 May 1998 and serves as priority founding application for the subsequently filed PCT application, filed on 28 May 1999.

The family relates to recombinant adeno-associated viruses, for use in gene delivery. On information from the Company, this family protects aspects of the AMT-021 and AMT-090 programs.

On information from the Company, the licensed portfolio of patents and applications at the last review was at least the rights listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in May

2019, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in European countries No. 1082413 Patent Application in Canada No. 2,329,060 Patent in the United States No. 6,984,517 Patent in the United States No. 7,479,554 Patent in Australia No. 762220 Patent Application in Japan No. 2000550986

On the basis of the cases that have proceeded to granted patents in strict examining Patent Offices of the world, Haseltine Lake LLP expects the currently pending applications to proceed to granted patents in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

## <u>In-Licensed Family E – AAV5 Vector for Transducing Brain Cells and Lung Cells</u>

On information from the Company, this family consists of US Patent No. 6,855,314. The patent document is available at http://gb.espacenet.com/search97cgi/s97\_cgi.exe?Action=FormGen&Template=gb/en/number.hts.

The PCT application was filed in the name of Government of the United States of America, Department of Health and Human Services and University of Iowa Research Foundation. On information from the Company, the rights are now owned by Government of the United States of America, Department of Health and Human Services. A license to use the technology has been obtained.

A US patent application (No. 09/533427) was filed on 22 March 2000 and US Patent No. 6,855,314 was granted on that application on 15 February 2005.

The family relates to recombinant adeno-associated viruses, for use in gene delivery to alveolar and cerebellar cells. On information from the Company, this family protects aspects of the AMT-090 program.

The US Patent has a potential expiry date in March 2020, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

On the basis that this patent has been granted in a strict examining Patent Office, namely the US Patent Office, we are not aware of any reason why the granted patent should be unenforceable in a court of law.

<u>In-Licensed Family F – Spodoptera Frugiperda Single Cell Suspension Cell Line in Serum-Free Media, Methods of Producing and Using</u>

This family is based on International (PCT) Patent Application No. PCT/US99/22862 (Publication No. WO-A-00/20561). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the name of Protein Sciences Corporation. On information from the Company, the rights are still owned by Protein Sciences Corporation. A license to use the technology has been obtained.

A US patent application (No. 09/169178) was filed on 8 October 1998 and serves as priority founding application for the subsequently filed PCT application, filed on 4 October 1999.

The family relates to insect cells useful as host cells for a recombinant baculovirus expression system. On information from the Company, this family protects aspects of the Company's general manufacturing platform, relevant or potentially relevant to all products

On information from the Company, the licensed portfolio of patents and applications at the last review was at least the rights listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in October 2019, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in European countries No. 1119612

Patent Application in Canada No. 2,346,497 Patent in the United States No. 6,103,526

On the basis of the cases that have proceeded to granted patents in strict examining Patent Offices of the world, Haseltine Lake LLP expects the currently pending application to proceed to granted patent in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

#### *In-Licensed Family G – RNA Export Element and Methods of Use*

This family is based on International (PCT) Patent Application No. PCT/US98/19441 (Publication No. WO-A-99/14310). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the name of The Salk Institute for Biological Studies. On information from the Company, the rights are still owned by The Salk Institute for Biological Studies. A license to use the technology has been obtained.

A US patent application (No. 08/936476) was filed on 18 September 1997 and serves as priority founding application for the subsequently filed PCT application, filed on 17 September 1998.

The family relates to recombinant vectors incorporating a nucleic acid – known as the woodchuck post-translational regulatory element or WPRE - that assists RNA export from the nucleus. On information from the Company, this family protects aspects of the GLYBERA® product.

On information from the Company, the relevant current portfolio of patents and application is listed below. While there may be a few exceptions, due to possible specific provisions of national laws which prescribe a patent term other than 20 years counted from the filing date of the application, the majority of these patents (or, subject to grant in due course, the applications) have a potential expiry date in September 2018, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in European countries No. 1017785 Patent Application in Canada No. 2,329,060 Patent in Australia No. 751326

Corresponding US Patent No. 6,136,597 was granted on Application No. 08/936476. This US patent is expected to expire in September 2017.

Related US Patents Nos. 6,284,469, 6,312,912 and 6,287,814 have also been granted to The Salk Institute. On information from the Company, a license to use this technology has also been obtained. The last of these patents is expected to expire in June 2020.

On the basis of the cases that have proceeded to granted patents in strict examining Patent Offices of the world, Haseltine Lake LLP expects the currently pending application to proceed to granted patent in due course and we are not aware of any reason why the granted patents should be unenforceable in a court of law.

## <u>In-Licensed Family H – GlialDerived Neurotrophic Factor Technology</u>

A family of rights relating to glial derived neurotrophic factor (GDNF) technology has been licensed from a major pharmaceutical company. On information from the Company, this family protects aspects of the AMT-090 program.

Confidentiality obligations entered into by the Company prevent detailed disclosure in this Report.

# <u>In-Licensed Family I – Chimeric snRNA Molecules Carrying Antisense Sequences</u>

This family is based on International (PCT) Patent Application No. PCT/IT03/00273 (Publication No. WO-A-03/095674). The international patent application document is available at http://www.wipo.int/pctdb/en/.

The PCT application was filed in the name of Universita degli Studi di Roma. On information from the Company, the rights are still owned by Universita degli Studi di Roma, from whom a license to use the technology has been obtained.

One Italian patent application (No. RM2002A000253) was filed on 8 May 2002 and serves as priority founding application for the subsequently filed PCT application, filed on 6 May 2003.

The family relates to a gene that codes for an snRNA carrying an antisense sequence complementary to a splice junction. On information from the Company, this family protects aspects of the AMT-080 program.

On information from the Company, the licensed portfolio of patents and applications at the last review was at least the rights listed below. This patent in the different European countries has a potential expiry date in May 2023, subject to continued payment of the periodic renewal fees and subject to any extension to compensate for regulatory delay in obtaining drug approval.

Patent in European countries No. 1501931.

On the basis that this case has proceeded to granted patents in a strict examining Patent Office, namely the European Patent Office, we are not aware of any reason why the granted patents should be unenforceable in a court of law.

## <u>In-Licensed Family J – Gene Therapy Vectors</u>

A family of rights relating to gene therapy vectors has been licensed from a US research institution. On information from the Company, this family protects aspects of the AMT-060 program.

Confidentiality obligations entered into by the Company prevent detailed disclosure in this Report.

## In-Licensed Family K - Compositions and Methods for Detecting T Cell Mediated Immune Responses

A family of rights relating compositions and methods for detecting T cell mediated immune responses has been licensed from a biotechnology research institution. On information from the Company, this technology is of potential use in research.

On information from the Company, the family does not affect any current products of the Company.

Confidentiality obligations entered into by the Company prevent detailed disclosure in this Report.

#### In-Licensed Family L - AAV Transduction of Myoblasts

A family of rights relating AAV transduction of myoblasts has been licensed from a biotechnology company. On information from the Company, this family protects aspects of the GLYBERA® product.

Confidentiality obligations entered into by the Company prevent detailed disclosure in this Report.

## 4. Review and Analysis of the Company's Trade Mark Portfolio

We list below the Company's trade marks according to the information supplied by the Company. As far as we are aware, no other trade mark applications or registrations exist other than those shown below.

We note that the first right on the table below is registered in the name of AMT B.V., On information from the Company, advice has been received that the ownership can be regularised into the Company, Amsterdam Molecular Therapeutics (AMT) B.V., and this action will be taken at the earliest convenient opportunity.

Mark	Country	Class	Appl. No	Appl. date	Reg. No.	Reg. date	Ren. date	Applicant/ Proprietor	Status
AMT	Canada	01, 05, 42	1130879	12-2- 02.	630501	19-1-05.	19-1-20.	AMT B.V.	Registered

AMT	EU	01, 05, 42	2573137	11-2- 02.	2573137	3-7-03.	11-2-12.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
AMT and device	Benelux	01, 05, 42	996845	13-9- 01.	700080	13-9-01.	13-9-11.	AMT B.V.	Registered
AMT	Canada	01, 05, 42, 44	1478301	23-4- 10.				Amsterdam Molecular Therapeutics (AMT) IP B.V.	Pending
AMT	EU	01, 05, 42, 44	8640237	26-10- 09.	8640237	10-5-10.	26-10- 19.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
AMT	US	01, 05, 42, 44	85/02185 7	23-4- 10.				Amsterdam Molecular Therapeutics (AMT) IP B.V.	Pending
AMT	Switzer- land (WO)	01, 05, 42, 44	8640237- 01	23-4- 10.	1040425	23-4-10.	23-4-20.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
amt. delivering cure and device	Switzer- land	05	53615200 8	6-4- 09.	587323	9-6-09.	6-4-19.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
amt. delivering cure and device	Israel	05	209906	24-3- 08.	209906	7-2-10.	24-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
amt. delivering cure and device	Iceland	05	10692009	22-4- 09.	3772009	2-6-09.	2-6-19.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
amt. delivering cure and device	Jordan	05	100494	23-4- 08.	100494	23-4-08.	23-4-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered

amt. delivering cure and device	Norway	05	20090508	21-4- 09.	251774	14-7-09.	14-7-19.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
amt. delivering cure and device	Turkey	05	20092533	18-5- 09.	2009253	4-5-10.	18-5-19.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
amt. and device	EU	01, 05, 42, 44	8640252	26-10- 09.	8640252	10-5-10.	26-10- 19.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
amt. and device	US	01, 05, 42, 44	85/02190 8	23-4- 10.				Amsterdam Molecular Therapeutics (AMT) IP B.V.	Pending
DELIVERING CURE	Arab Emirates	05	113972	3-6- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Bahrain	05	64727	18-3- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Canada	5	1388257	20-3- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Egypt	05	215107	8-4- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Iran	05	86122678	18-3- 08.	157479	14-9-08.	18-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
DELIVERING CURE	Japan	05	20080230 29	27-3- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending

DELIVERING CURE	Lebanon	05	2449	8-4- 08.	116062	24-4-08.	24-4-23.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
DELIVERING CURE	Libya	05	17093	5-2- 09.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Morocco	05	118083	19-6- 08.	118083	17-11- 08.	19-6-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
DELIVERING CURE	Oman	05	49398	19-3- 08.	49398	11-8-09.	19-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
DELIVERING CURE	Qatar	05	50165	3-4- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Russian Feder- ation	05	20087074 90	14-3- 08.	381651	16-6-09.	14-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
DELIVERING CURE	Saudi Arabia	05	129350	19-4- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Syria	05	3814	22-4- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	Tunisia	05	EE08075 5	19-3- 08.	EE0807 55	26-1-10.	19-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
DELIVERING CURE	US	05	77/42159 0	13-3- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
DELIVERING CURE	South Africa	05	20080583 6	14-3- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
G and device	EU	05, 44	8640609	26-10- 09.	8640609	10-5-10.	26-10- 19.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
G and device	US	05, 44	85/02193 8	23-4- 10.				Amsterdam Molecular Therapeutics (AMT) IP B.V.	Pending

GLYBERA	Arab Emirates	05	101941	31-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	Australia	05	1176048	14-5- 07.	1176048	12-12- 07.	14-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Bahrain	05	62689	7-1- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	Canada	5	1355754	16-7- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	Switzer- land	05	55139200 7	14-5- 07.	562178	11-9-07.	14-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Algeria	05	72791	24-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	Egypt	05	208229	22-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	EU	05, 44	5901269	1-5- 07.	5901269	14-5-09.	1-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Israel	05	204800	21-10- 07.	204800	11-8-09.	21-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Iceland	05	14642007	14-5- 07.	8122007	4-7-07.	4-7-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Jordan	05	99133	24-10- 07.	99133	1-5-07.	1-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Japan	05	20070542 57	30-5- 07.	5088657	2-11-07.	2-11-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Lebanon	05	6612	23-10- 07.	113370	25-10- 07.	25-10- 22.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Libya	05	16593	22-12- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending

GLYBERA	Morocco	05	113550	23-10- 07.	113550	23-10- 07.	23-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Norway	05	20070560	15-5- 07.	241553	19-10- 07.	19-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	New Zealand	05	768310	14-5- 07.	768310	15-11- 07.	14-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Oman	05	47462	22-10- 07.	47462	24-8-08.	22-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Qatar	05	47253	31-10- 07.	47253	31-12- 09.	31-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Russian Feder- ation	05	20087073 40	13-3- 08.	377215	20-4-09.	13-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Saudi Arabia	05	125692	12-1- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	Syria	05	4268	28-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	Tunisia	05	EE07266 7	24-10- 07.	EE0726 67	19-5-09.	24-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	Turkey	05	20070267 78	17-5- 07.	2007267 78	17-5-07.	17-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
GLYBERA	US	05	77/17935 6	11-5- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
GLYBERA	South Africa	05	20072391 9	19-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
Glybera and device	EU	05, 44	8640641	26-10- 09.	8640641	10-5-10.	26-10- 19.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
Glybera and device	US	05, 44	85/02198 5	23-4- 10.				Amsterdam Molecular Therapeutics (AMT) IP B.V.	Pending

LPLCHIP	Canada	1, 10, 42, 44, 5, 9	1474070	22-3- 10.				Amsterdam Molecular Therapeutics (AMT) IP B.V.	Pending
LPLCHIP	EU	01, 05, 09, 10, 42, 44	8590911	2-10- 09.	8590911	31-5-10.	2-10-19.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
LPLCHIP	US	1, 5, 9	77/96489 2	22-3- 10.				Amsterdam Molecular Therapeutics (AMT) IP B.V.	Pending
LPLCHIP	Switzer- land (WO)	01, 05, 09, 10	8590911- 01	6-4- 10.	1036745	6-4-10.	6-4-20.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
LPLCHIP	Iceland (WO)	01, 05, 09, 10	8590911- 01	6-4-10.	1036745	6-4-10.	6-4-20.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
LPLCHIP	Norway (WO)	01, 05, 09, 10	8590911- 01	6-4- 10.	1036745	6-4-10.	6-4-20.	Amsterdam Molecular Therapeutics (AMT) IP B.V.	Registered
VECTIPRO	Arab Emirates	05	101942	31-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	Australia	05	1176051	14-5- 07.	1176051	12-12- 07.	14-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Bahrain	05	62690	7-1- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	Canada	5	1355761	16-7- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	Switzer- land	05	55138200 7	14-5- 07.	562177	11-9-07.	14-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Algeria	05	72793	24-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	Egypt	05	208203	22-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	EU	05	5901277	1-5- 07.	5901277	10-4-08.	1-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered

VECTIPRO	Israel	05	204915	23-10- 07.	204915	11-8-09.	23-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Iran	05	86091403	8-12- 07.	157475	14-9-08.	8-12-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Iceland	05	14632007	14-5- 07.	8112007	4-7-07.	4-7-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Jordan	05	99366	24-10- 07.	99366	14-1-09.	1-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Japan	05	20070542 58	30-5- 07.	5088658	2-11-07.	2-11-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Lebanon	05	6622	23-10- 07.	113434	30-10- 07.	30-10- 22.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Libya	05	16595	22-12- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	Morocco	05	113551	23-10- 07.	113551	23-10- 07.	23-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Norway	05	20070560 4	15-5- 07.	241558	22-10- 07.	22-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	New Zealand	05	768309	14-5- 07.	768309	12-2-09.	1-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Oman	05	47461	22-10- 07.	47461	30-5-09.	22-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Qatar	05	47255	31-10- 07.	47255	31-12- 09.	31-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	Russian Feder- ation	05	20087073 42	13-3- 08.	381400	10-6-09.	13-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Saudi Arabia	05	125693	12-1- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending

VECTIPRO	Syria	05	4269	28-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
VECTIPRO	Tunisia	05	EE07266 6	24-10- 07.	EE0726 66	19-5-09.	24-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	Turkey	05	20070267 79	17-5- 07.	2007267 79	17-5-07.	17-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	US	05	77/17935 7	11-5- 07.	3703954	3-11-09.	3-11-19.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
VECTIPRO	South Africa	05	20072391 8	19-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	Arab Emirates	05	101943	31-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	Australia	05	1176049	14-5- 07.	1176049	12-12- 07.	14-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Bahrain	05	62691	7-1- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	Canada	5	1355762	16-7- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	Switzer- land	05	55198200 7	15-5- 07.	562360	13-9-07.	15-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Algeria	05	72792	24-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	Egypt	05	208231	22-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	EU	05, 44	5901251	1-5- 07.	5901251	22-1-09.	1-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Israel	05	204799	21-10- 07.	204799	11-4-09.	21-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered

ZYAMTIN	Iran	05	86091401	8-12- 07.	158201	14-9-08.	8-12-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Iceland	05	14652007	14-5- 07.	8132007	4-7-07.	4-7-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Jordan	05	99208	24-10- 07.	99208	3-3-09.	1-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Japan	05	20070542 59	30-5- 07.	5088659	2-11-07.	2-11-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Lebanon	05	6623	23-10- 07.	113437	30-10- 07.	30-10- 22.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Libya	05	16594	22-12- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	Morocco	05	113552	23-10- 07.	113552	23-10- 07.	23-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Norway	05	20070560 5	15-5- 07.	2007056 05	18-10- 07.	18-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	New Zealand	05	768311	14-5- 07.	768311	15-11- 07.	14-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Oman	05	47463	22-10- 07.	47463	30-5-09.	22-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Qatar	05	47254	31-10- 07.	47254	31-12- 09.	31-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Russian Feder- ation	05	20087073 41	13-3- 08.	394999	1-12-09.	13-3-18.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Saudi Arabia	05	125694	12-1- 08.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	Syria	05	4267	28-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending

ZYAMTIN	Tunisia	05	EE07266 8	24-10- 07.	EE0726 68	19-5-09.	24-10- 17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	Turkey	05	20070267 80	17-5- 07.	2007267 80	7-4-08.	17-5-17.	Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Registered
ZYAMTIN	US	05	77/17935 9	11-5- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending
ZYAMTIN	South Africa	05	20072391 7	19-10- 07.				Amsterdam Molecular Therapeutics (AMT) Holding N.V.	Pending

As far as we are aware, the trademarks listed above are validly registered and we expect that the applications will proceed to registration.

#### 5. Third Party Activities

## Third Party Patent and Trade Mark Rights

On information from the Company, the Company is not currently opposing any third party patents or patent applications in any country. On information from the Company, no third party is currently opposing any of the Company's patents or patent applications in any country.

On information from the Company, the Company is not currently opposing any third party trade marks in any country. On information from the Company, a third party has opposed the application for GLYBERA® in the United Arab Emirates, and the action is being defended. Other than that there are no challenges to the Company's right to own and use listed trade marks.

# **Unauthorised Third Party Use**

On information from the Company, no actions for patent infringement have been filed against any third parties and the Company is not aware of any unauthorised third party use of its inventions.

On information from the Company, no actions for trade mark infringement are currently being pursued by the Company against any third parties, and the Company is not aware of any unauthorised third party use of its trade marks.

Yours faithfully

David L. Brown, for **HASELTINE LAKE LLP** 

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## REGISTERED OFFICE OF THE COMPANY

# Amsterdam Molecular Therapeutics (AMT) Holding N.V.

Meibergdreef 61 1105 BA Amsterdam Zuidoost The Netherlands

# **LEGAL ADVISORS TO THE COMPANY**

As to Dutch law

As to United States law

**Simmons & Simmons** 

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#### **INDEPENDENT AUDITORS**

# PricewaterhouseCoopers Accountants N.V.

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