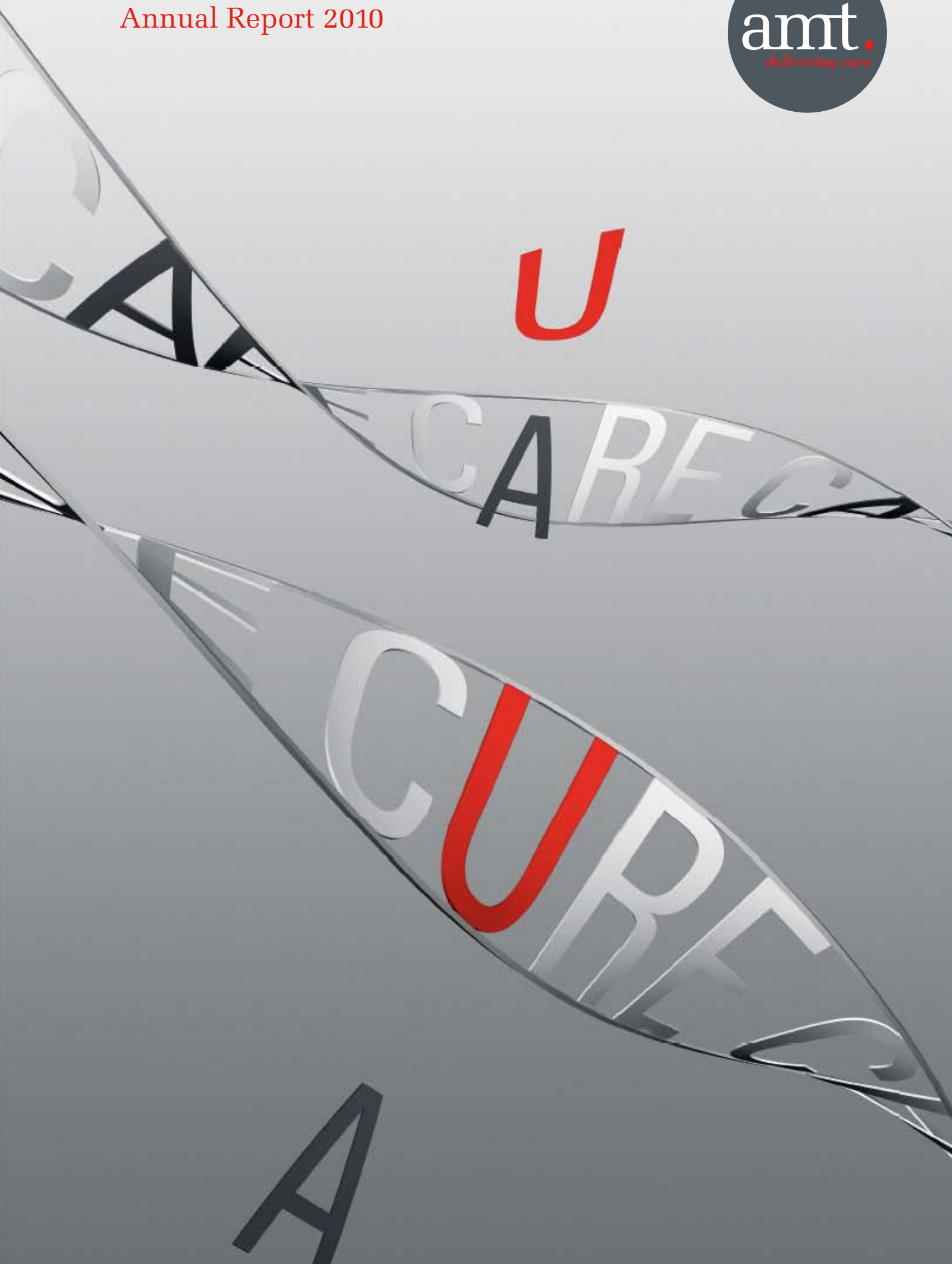


# Annual Report 2010



# Key Data

Amounts in € x 1,000, except per share data

	31.12.2010	31.12.2009
Total net income	1,448	355
Research and development costs	(16,404)	(13,241)
General and administrative costs	(4,113)	(4,913)
Total operating costs	(20,517)	(18,154)
Operating result	(19,069)	(17,799)
Result for year	(19,118)	(17,175)
EPS	(1.13)	(1.17)
Cash	17,859	22,624
Equity	13,659	18,410

# From Care to Cure

There are approximately 7000 inherited orphan diseases known to date of which only 200 are treatable with the current drugs approved. Orphan diseases are both rare and life threatening and patients have to rely on constant medical care to manage their complaints. The challenge for companies developing orphan drugs is in the development process, which is similar to non-orphan drugs, but the comparable costs are much higher because of the small number of patients. Overall, the regulatory agencies are increasingly supportive for simplifying the process but there is a line they cannot cross in the context of their legal framework. The introduction of a complete orphan drug legislation, allowing for short-cuts in development, would make a big difference in generating solutions for companies and ultimately many patients.

AMT is dedicated to improve the lives of patients suffering from orphan diseases. To this end the Company has developed a unique gene therapy platform, which has the potential to become the therapeutic approach of choice for inherited disorders, and has the first orphan disease product in European registration. AMT is proud to be the leading Company providing patients with real long-term cures based on this approach.



# Letter to Shareholders

“We are excited by the key milestones achieved in 2010: our lead product Glybera® is progressing towards market approval and we are looking forward, with confidence, to the Regulatory Agency’s decision. We have continued, also, to make good progress in our other pipeline programs, on both the partnering and scientific fronts.”

## **Activities in 2010 were Focused on Advancing our Lead Product Glybera® along the Path to Marketing Authorization**

We are delighted to have the first product from our internal research – Glybera® to treat lipoprotein lipase (LPL) deficiency – successfully developed all the way through to the marketing authorization process. The route to registration for an innovative product such as Glybera® is extremely important, not only for AMT, but also for thousands of patients suffering from rare diseases. Marketing approval will validate AMT’s unique adeno-associated viral (AAV) vector delivery platform which can then be used to deliver other gene therapy products for other indications. Gene therapy has the potential to become the therapeutic approach of choice to improve the lives of patients suffering from inherited disorders; we are proud to be the leading Company promising patients real long-term cures based on this approach.

## The Highlights of 2010

### **Glybera® on Track for a Regulatory Decision in Mid-2011**

Advancing our lead product Glybera® towards market approval was certainly the major focus of our activities during 2010, and the regulatory process continues to progress on schedule. Following the filing of Glybera® with the European Medicines Agency (EMA) the agency conducted its initial review of the Glybera® registration dossier in early 2010 and sent the Day 120 List of Questions to AMT in May. We submitted our response to the EMA in November 2010, based in part on additional data and analyses from patients previously treated with Glybera®, including new data available from the last clinical trial and its one-year extension. The EMA restarted evaluation on November 26 (Day 121), and we have received, at Day 180, a further list of questions summarizing the outstanding items following the EMA’s review of our responses.

Our dialogue with the EMA is very encouraging and we confidently look forward to their decision. Our confidence in the approvability of Glybera® is based on three important facts: (i) we do not need further clinical trials with additional new

## Letter to Shareholders

patients; (ii) we have identified a biomarker that strongly suggests Glybera's® effects are long-lasting; and (iii) we have developed a clear response strategy, which if executed with no unforeseen events or delays, should allow us to remain on track for a positive regulatory response in mid 2011.

### **Novel Biomarker for Glybera® Activity Identified**

AMT is conducting long-term follow up studies on two LPL deficiency clinical trials in Europe and Canada and a further ongoing trial in Canada. In these three studies a single dose of Glybera® has shown an excellent safety profile and a significant decrease in the incidence of acute pancreatitis, the most debilitating complication of LPL deficiency.

Encouragingly, in 2010 new clinical data from the ongoing clinical study in Canada provided evidence for explaining the mechanism of action of Glybera®, and in general for continued long-term clinically relevant pharmacological activity after one-time gene therapy treatment which we believe will strongly support the upcoming regulatory response.

### **Pipeline of Orphan Projects Progressing – Focus on Partnering Remains an Important Value Driver**

In 2009, we refocused our corporate strategy to make sure AMT developed high priority programs to important value inflection points. To this end, we decided to focus our activities on accelerating the development of our, primarily orphan, pipeline products; combining both proprietary and partnered development. Our programs achieved important milestones during the year and, the potential approval of Glybera® will free up resources to accelerate further the development of these additional promising programs.

### **Hemophilia B Advanced to Clinical Development – First Results of Phase I/II Study Encouraging**

In March 2010, AMT's partner St Jude Children's Research Hospital started dosing patients in an exploratory Phase I/II clinical trial with a gene therapy product for hemophilia B, a seriously debilitating and potentially lethal bleeding disorder. The objective of the trial is to assess the safety and efficacy of different doses of hemophilia B gene therapy. Initial data demonstrate good results both in terms of clinical benefit based on long-term stable expression and side effects. This hemophilia B gene therapy, administered just once, introduces the functional gene for the Factor IX protein into a patient's liver cells with the goal of restoring long-term blood clotting functionality. AMT has a license and commercial rights to the gene.

### **GDNF Gene License Agreement Amended with Amgen**

In December 2010, AMT amended its licensing agreement with Amgen for gene therapy applications incorporating the glia cell derived neurotrophic factor (GDNF)

gene to which Amgen holds rights. The GDNF gene contains the information to produce a protein necessary for the development and survival of nerve cells. Studies with a GDNF gene therapy, AMT-090, in a Parkinson's disease (PD) model are being conducted by AMT in collaboration with the University of Lund, Sweden. Based on promising early results of this approach, AMT believes there is an opportunity for a similar approach in a range of CNS disorders with the aim to protect and enhance the function of affected nerve cells. To this end, AMT has renegotiated its agreement with Amgen that now allows AMT to progress the GDNF program also in alternative gene therapy applications such as Huntington's disease or Multiple System Atrophy (MSA).

#### **FDA Orphan Drug Designation for Duchenne Muscular Dystrophy Product**

Duchenne Muscular Dystrophy (DMD) is a fatal disease causing progressive weakening of the muscles. In September 2010, the U.S. Food and Drug Administration (FDA) designated gene therapy candidate AMT-080 as an orphan drug to treat DMD. It is exceptional that we have been able to reveal the promise of this therapy to the FDA at this early stage of development. As a designated orphan drug, AMT-080 is eligible for tax credits based on its clinical development costs, as well as assistance from FDA in guiding the drug through the regulatory approval process.

#### **Porphyria Grant Funding as Part of EU Consortium Finalized**

In January 2011, the EU finalized a €3.3 million grant to the AIPGENE consortium, of which AMT is a member, for the development of a gene therapy product for Acute Intermittent Porphyria (AIP). AIP is a severe and progressive disease caused by the inability of the body to produce the heme protein, a component of hemoglobin, as well as other important proteins. AMT holds the commercialization rights to an AIP gene therapy (AMT-021). From the grant AMT will receive €1.1 million. It will cover approximately 75% of AMT's overall development costs to bring this product forward to completion of a Phase I/II study in humans. With the support of all the AIPGENE partners, AMT anticipates AIP patient enrolment in a clinical trial to begin in 2012.

In early 2011, we expanded our pipeline with an additional program:

#### **AMT to Join Forces with a Consortium Led by Institut Pasteur for Development of a Sanfilippo B Gene Therapy**

In January, AMT entered into an agreement with the Institut Pasteur and a group of French research institutes to support clinical development of a novel gene therapy to treat SanfilippoB, a rare genetic disease affecting new-born children and leading to progressive neuronal degeneration and death. Institut Pasteur will lead the development program and will also sponsor a Phase I/II clinical study. Initially, AMT will manufacture and supply the gene therapy product, receiving payments of up to €1.8 million. In addition, AMT will have the right to acquire the full commercial rights to the program once the consortium demonstrates proof-of-concept in the Phase I/II study.

## Letter to Shareholders

This is a strong, risk-free alliance for AMT to exploit the broad potential of its gene therapy platform and deliver a cure for patients with very challenging diseases.

### Increased Financial Flexibility through € 14.3 Million Financing

To fund Glybera® further through its regulatory and commercial development and to continue the development of the hemophilia B and other pipeline programs, we have increased our financial flexibility significantly during the year. On October 6, AMT successfully raised € 14.3 million through the sale of 8.4 million new ordinary shares at € 1.70 each. Investors included major shareholders Advent Venture Partners, Crédit Agricole Private Equity, Forbion Capital Partners and Gilde Healthcare Partners, plus AMT management. In addition, we received an innovation credit of € 4 million from the Dutch government's Innovation Agency, in January 2010, for the development of our DMD treatment. The credit will fund 35% of all the development costs of this project through mid 2013. The loan is repayable only if AMT successfully commercializes the product.

In summary, we are focusing on the successful completion of the Glybera® registration process in 2011, and AMT has strong potential to be the first company to introduce successfully a safe and efficacious gene therapy product. As gene therapy carries the promise to cure a range of diseases caused by a single gene, we will make every effort to reach the market with this unique product, validate our approach and open the door to future innovative therapeutic solutions for the very substantial number of patients suffering from serious challenging inherited diseases.

We are grateful for having the opportunity to advance this vision with you and with the enthusiastic team at AMT, a strong executive management team in place and the loyalty of our shareholders.



Ferdinand Verdonck  
Chairman



Jörn Aldag  
Chief Executive Officer



# The Future of Orphans

On a conservative count, there are approximately 7000 rare diseases known to date, of which only about 200 are currently treatable with one of the 360 orphan drugs approved globally since 1983. In the US and Europe alone, 70 million people are estimated to suffer from rare diseases. The issue today is how companies can be encouraged to develop drugs for the currently non-treatable rare diseases and still make profits healthy enough to attract investor support. The answers are manifold but one important aspect is the regulatory approvals process for these orphan drugs and the future of therapeutic development technologies.

The current regulatory environment, though supportive of orphan drug development, could do more to help drive the discovery and development of orphan drugs. The following is a discussion between Ulrich Granzer, Chairman of the German Association of Regulatory Affairs (DGRA) and Owner of Granzer Regulatory Consulting & Services and Jörn Aldag, Chief Executive Officer of Amsterdam Molecular Therapeutics.

## **What are the major issues facing companies developing orphan drugs, today?**

Ulrich Granzer: “There are several issues facing these companies but the most important concern is patient recruitment. The regulatory requirements for orphan and ultra orphan drugs, with very small global populations, are similar when compared to any other drug development. For instance the FDA requires two pivotal controlled trials to obtain a marketing authorisation; if you only have a few hundred patients worldwide, this is a real issue. This may be slightly easier in Europe, but still, the classical approval requirements remain, for instance a p value equal to 0.05 or better, which typically requires several hundred patients in such a trial.”

Jörn Aldag: “AMT’s lead product Glybera for Lipoprotein Lipase Deficiency (LPLD) is currently under review in the centralized procedure. We expect an opinion from the regulatory authorities in the summer of 2011. In our experience, patient recruitment for novel therapeutic approaches in the rare disease area is a real challenge. For LPLD, we expect that there are fewer than 1,000 patients worldwide and less than 500 in Europe who could potentially benefit from a gene therapy treatment. We would never have found several hundred patients. Our file is based on only 27 patients from 3 clinical trials. In our experience, though, while they would have preferred much larger numbers, the regulatory agencies (in this case the CAT, Committee for Advanced Therapies) are willing to accept such a small number and do not seem to request further clinical trials with additional patients.”

Ulrich Granzer: “The issue with small patient populations is that you can’t easily do Phase IIa, Phase IIb or Phase III trials where you can develop meaningful end points. If you have a very limited number of patients it is always difficult to validate those endpoints, especially if you are the first in the field.”

Jörn Aldag: “Yes, validating endpoints is very difficult in the context of small clinical trials. Trials will have to become more flexible while they are being performed. It will also be necessary, that the regulatory agencies appreciate there is a lot of

## The Future of Orphans

learning during trials, knowledge gathering that you would normally expect to happen before the definitive (pivotal) trials. And in the case of very rare diseases, there may be no other way than to accept post-hoc defined primary endpoints.”

Ulrich Granzer: “Another major issue is the return on investment (ROI) for orphan drugs. Development in all phases is comparable to non-orphan drugs, especially in terms of toxicology, chemistry and pharmacy studies. This means that the development cost for orphan drugs will always be much higher than for non-orphan drugs because of the small number of patients. In turn, this limits the potential ROI for an orphan drug.”

Jörn Aldag: “There is a clear correlation between development cost and the pricing for a rare disease drug. If the regulatory process remains like it is, then pricing for orphans will continue to be very high. If you want more therapies for rare diseases and if you want high regulatory scrutiny, then you have to accept that prices for orphans have to be much higher than for other drugs.”

### **What are the current arguments addressing the regulatory environment for orphan drug development?**

Ulrich Granzer: “In addition to the above mentioned issues there are discussions on clinical endpoints, pricing, reimbursement and new regulations for ultra orphan drugs compared to orphan drugs. The issue with clinical endpoints is significant for orphan drugs and we always discuss these with the regulators. They usually do not deviate from requirements for the chemistry, pharmacology or the preclinical toxicology development as there is no shortage in resources other than money. These discussions focus on what are the clinical endpoints, what kind of clinical endpoints regulators need; do they need outcome endpoints, are surrogate markers, biomarkers, etc. adequate? The validity of the endpoints, the p value of the primary endpoint or co-primary endpoints or of more than one primary endpoint and the value of secondary endpoints? If a company is developing a new cardiovascular drug for the reduction of blood pressure you have all the parameters from previous studies by other groups. When developing new orphan drugs, companies have to define what a predictive endpoint might be and what it might look like.”

Jörn Aldag: “I guess that the regulators’ hands are tied in this regard. From our Glybera experience, the key thing would have been to know upfront that they would accept an endpoint that is more precisely defined in a post-hoc analysis and that it is very critical for them to measure biomarkers or surrogate markers. A sheer clinical outcome endpoint in the context of small patient numbers in the trial seems to be inadequate.”

Ulrich Granzer: “We have to focus on the issues of clinical development, the reduction in the number of patients to be included in trials. These are all items that also need to be discussed. Overall, regulatory agencies are very cooperative but there is a line they cannot cross in the context of their legal framework.”

**What major changes could healthcare regulatory agencies implement that would support biotech companies in advancing orphan drug candidates to the market?**

Jörn Aldag: “We believe that they would need to work with the legislators on a specific orphan and ultra-orphan drug legislation which is distinct from the larger indications and which would give them larger freedom to operate in their decision making.”

Ulrich Granzer: “The regulatory agencies are currently stuck within a very rigid scaffold that needs to be removed for orphan drugs and especially ultra orphan drugs. Ultra orphan diseases include diseases like Hypertriglyceridemia, which has a couple of hundred patients worldwide. There is also Progeria, where the patients age very, very fast and die at the age of eight or nine when they look like a person of 100 years of age. There are only between 10 and 20 patients with Progeria in the EU. In Duchenne Muscular Dystrophy there are between 5 to 10 thousand patients worldwide. All these are horrible diseases that do need addressing with their own regulatory legislation.”

Jörn Aldag: “I find Progeria an interesting example, Ulrich. The prevalence of the disease is about 1:8.000.000. Obviously, this is an extreme, but why should you not be able to develop a gene therapy treatment for these poor patients if you knew upfront (i) that you would need no more than 5 patients in a Phase I/II trial to demonstrate safety, (ii) your price, and (iii) that you could run your Phase III trial under a ‘reimbursed named patient scheme’?”

Ulrich Granzer: “Interesting thought. Currently, the agencies offer scientific advice free of charge for orphan developments. They offer discussion whenever necessary and they are very supportive, but the regulators as such can do no more. It is more a question for politicians and the political world to support orphan drug development. Basically, politicians would have to allow the regulators to make decisions on lowering the thresholds for the chemistry, pharmacy and preclinical part of the development process. Additionally, they need to setup a complete Orphan Drug legislative framework that allows for short cuts in development. They could introduce simplified regulations for the development processes for orphan drugs where no treatment exists.”

**What policy could be introduced that would lower the risk of investing in companies specialising in orphan indications and what is the best approach to tailoring the current regulatory environment in favour of orphan drug companies to address this?**

Ulrich Granzer: “These questions are really the centre of all current discussions. The regulatory environment needs to be supplemented by real orphan drug legislation, not just ‘Orphan Drug designation’ where only the very first tiny step is supported. There needs to be legislation that allows for cost efficient development,

## The Future of Orphans

for instance, a lower threshold than current regulations permit. This will allow companies to cut back on preclinical studies but still get a sensible level of drug safety. This is the policy that has to come from the political arena and cannot come from regulators, nor from the pharma industry.”

Jörn Aldag: “I fully concur with this view.”

Ulrich Granzer: “Currently the FDA and EMA are reviewing their orphan drug policies, but these are internal regulatory authority policies that have to be interpreted in the framework of the current legislation and that’s the real issue, because the agencies can’t get out of the drug approval box, at this time. We need to find a strategy that can be taken up by politicians and that can change the current legislation for orphan drug development. It is Government that needs to focus on this issue. It is the high level contacts we need to address, and then to discuss legislation with the experts in the field. Highly reputed organisations, like for example the Wellcome Trust, the Gates Foundation and similar non-profit organisations, would be the right bodies to convey this message.”

### **Pricing is an issue for orphan drugs, are there any regulatory proposals that address this? If not, what would you propose?**

Ulrich Granzer: “Right now it is free pricing for practically all orphan drugs, and there is discussion about whether orphan drugs should go through a different pricing and reimbursement cycle. Currently, there is a policy, ‘The Health Technology Assessment’, to be implemented in Europe where all drugs have to show an additional benefit to a competitor. Clearly, most orphan drugs will have no or limited competition.”

Jörn Aldag: “The issue for gene therapy is that you deal with a novel treatment paradigm: one treatment, one cure – so, no life long treatment and revenue stream. We know from extensive market research that the reimbursement authorities seem to not only accept, but to suggest the idea of: multiply the number of years of proven efficacy by the price for other orphan drugs for similar diseases. Following their suggestion means accepting price levels in the 7-digit EURO range. LPLD is comparable to Gaucher Disease in terms of severity. We have 5 years of clinical benefit. So you multiply 5 years by the price of Cerezyme®, Genzyme’s Gaucher drug.”

Ulrich Granzer: “We do have two groups of orphan therapies; the ones targeting the ultra orphan diseases, and those targeting indications where the threshold for orphan designation is only just being met. This latter group can be developed and sold like classical drugs but with the orphan benefit, and these are the ones the pricing and reimbursement regulators are starting to focus on.”

Jörn Aldag: “And they should ...”

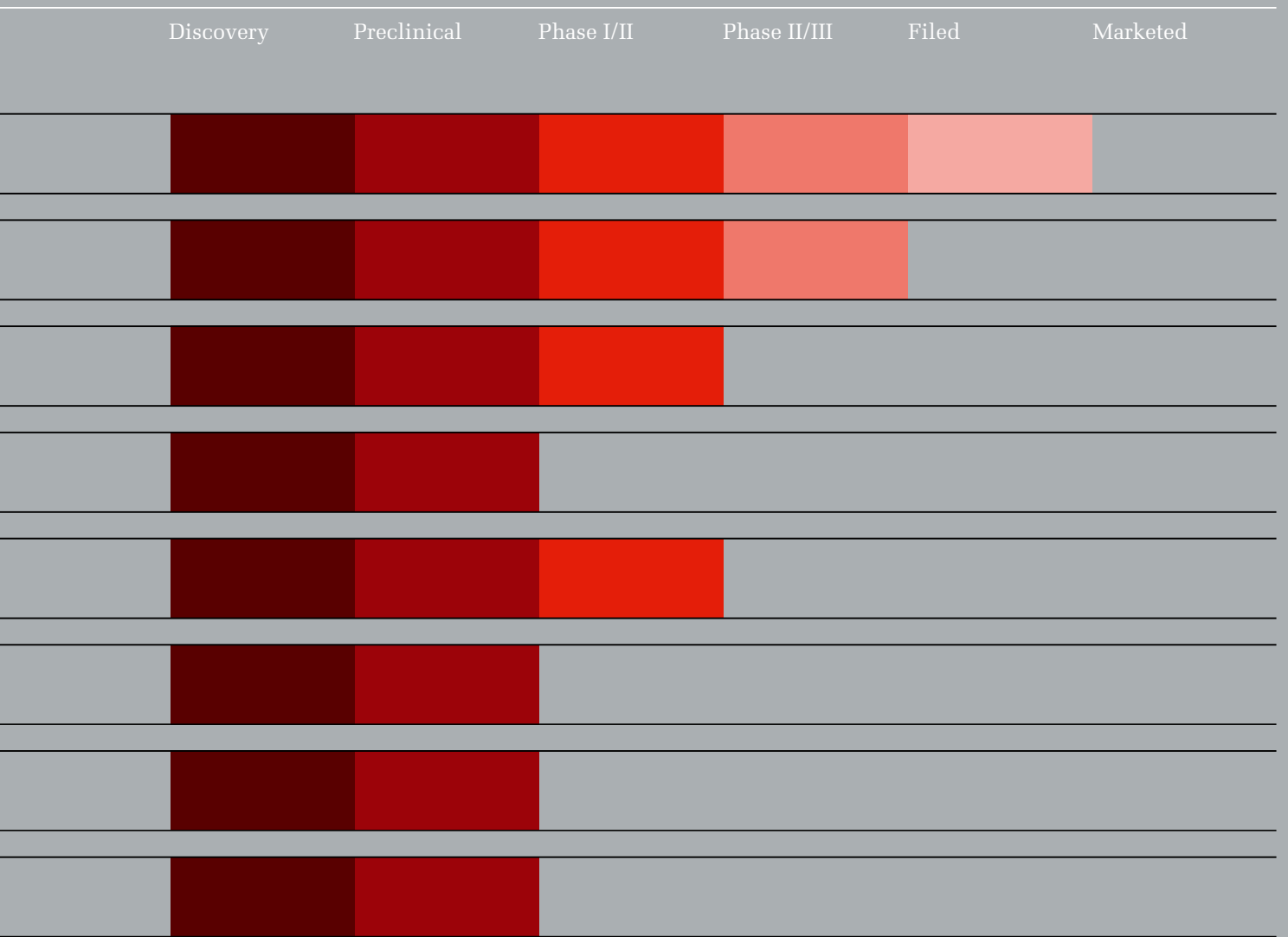
**What is a good approach to ensure the best environment of companies developing orphan drugs?**

Ulrich Granzer: “I think it is our politicians that need to act here. If our citizens and politicians do want to improve life for patients suffering from orphan diseases it is not sufficient to just reduce registration fees from EUR 250,000 to zero, which basically only pays for about eight patients in an orphan drug clinical trial. A change of legislation by taking a bit more risk would have to take place. Just one example: if you have to do three consecutive manufacturing runs of your product in order to get marketing approval that means you end up making products for 10,000 patients but only need to treat 300 patients, this makes little sense. Instead, it would be better to perform one run then two years later do a second run, but that means you do not fulfil the GMP requirement of three consecutive runs prior to launch. There are a lot of these issues where I am sure politicians and regulators would be supportive of simplifying the current regulations. The real importance is legislation for ultra orphan diseases. For this patient population the development thresholds need to be reduced and the regulatory authorities need to have the freedom to approve a product based on their expertise, even if not all the requirements are being fulfilled.”

# Product Pipeline

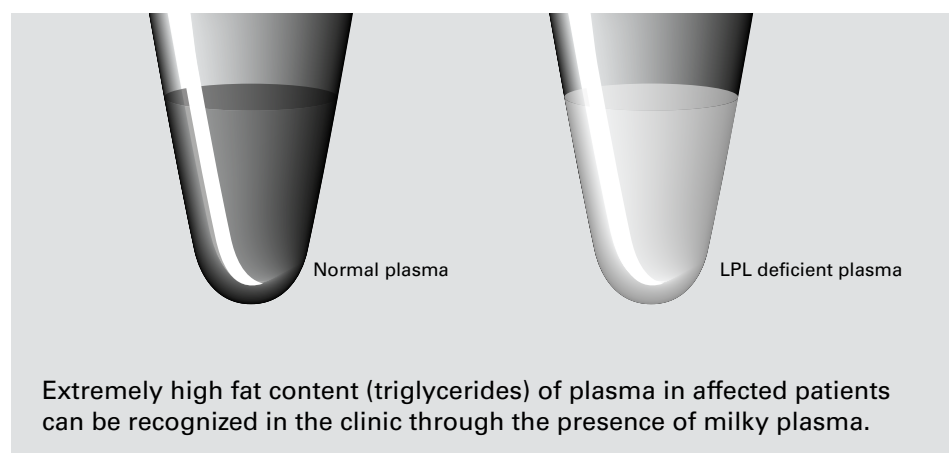
Program	Organ	Orphan designation
<b>Glybera® Europe</b>	Muscle	EU/US
<b>Glybera® US &amp; Canada</b>	Muscle	EU/US
<b>Glybera® HLP5</b>	Muscle	EU/US
<b>Duchenne Muscular Dystrophy</b>	Muscle	EU/US
<b>Hemophilia B</b>	Liver	–/–
<b>Acute Intermittent Porphyria</b>	Liver	EU/–
<b>Parkinson's Disease</b>	CNS	NA
<b>Sanfilippo (Institut Pasteur program)</b>	CNS	–/–

AMT's pipeline is focused on programs which are either aimed at orphan diseases for which no effective treatment is available (DMD, AIP, LPLD) or suited to cause breakthrough innovation and change of dynamics in diseases where the existing standard of care offers scope for significant improvement (Parkinson's disease, Hemophilia B).



### Lipoprotein Lipase Deficiency

LPLD is a seriously debilitating orphan disease caused by mutations in the LPL gene, resulting in highly decreased 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 (CM), accumulate in the blood, they may obstruct small blood vessels. The clinical result is recurrent and potentially lethal acute inflammation of the pancreas, called pancreatitis. The disease can also result in difficult-to-treat diabetes, an increased risk of cardiovascular complications, and is also associated with significant morbidity and mortality. There is no treatment for LPLD available and therapies are mostly through a restricted diet allowing virtually no fat but this does not entirely prevent the occurrence of pancreatitis and the other disease related complications. Glybera® is a gene therapy, which restores the LPL enzyme activity required to process the fat carrying particles.



### Novel Biomarker for Glybera® Activity Identified

The data package for Glybera® includes three clinical studies conducted in the Netherlands and in Canada, in which a total of 27 LPLD patients participated. Follow-up studies are ongoing. In all trials the therapy was well tolerated and safe. The data indicates that fat concentrations in blood were reduced after therapy in nearly all patients between 3 and 12 weeks after injection of Glybera®. Importantly, a single dose administration of Glybera® resulted in a long-term presence and biological activity of the protein in the injected muscle and the data indicated a clinically important reduction in the frequency of acute pancreatitis, the most debilitating complication of LPLD.

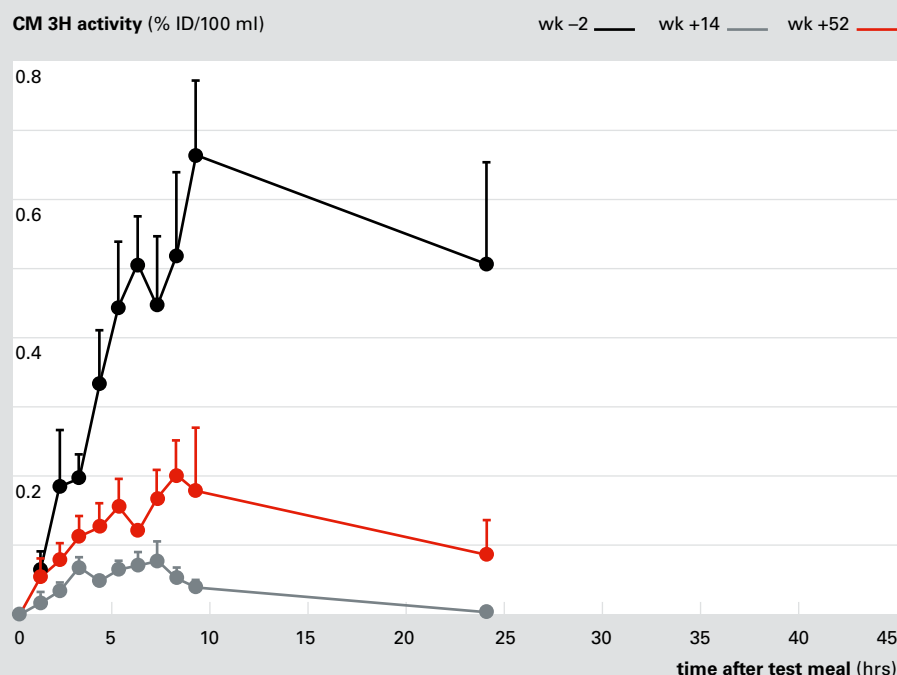
Encouragingly, new clinical data from the last clinical study in Canada provided a basis for explaining the mechanism of action of Glybera®. Also, the data provided evidence for long-term activity after one-time gene therapy, which represents an important clinical validation of the AAV gene therapy platform. The study results



indicate that a single administration of Glybera® in LPLD patients results in a remarkable long-term improvement in the ability to break down chylomicrons that transport dietary fat. LPLD patients are incapable of clearing chylomicrons which are responsible for causing significant morbidity and mortality. In particular, very high levels of chylomicrons produced after meals are thought to be the eliciting factor in new acute pancreatitis episodes.

### Results from 3<sup>rd</sup> Clinical Trial Regarding the Pharmacology of Glybera®

The 24 hour test shows that even a year after one-time Glybera® administration there is sufficient activity from the therapy to greatly improve the breakdown of lipids from a standard meal.



Note (CM 3H activity): A specific, radiolabelled fatty acid is used to follow the fate of dietary fat in the body over more than 24 hours.

**Before treatment** A standardized high-fat milkshake in the morning leads to excessive and persistent fat accumulation in plasma of untreated LPLD patients during 24 hours.

**14 weeks after treatment** Due to the treatment with Glybera®, the ability to reduce dietary fat in the circulation is greatly improved and the time profile in the plasma is normalized.

**1 year after treatment** Fat metabolism remains significantly improved in all tested patients one year after a single treatment with Glybera®.

“The long-term improvement in chylomicron handling following Glybera® administration is very impressive,” said Dr. Andre Carpentier, co-investigator from the University of Sherbrooke, Quebec, Canada, who designed and analyzed the chylomicron sub-study. “These data are important, because the major complications observed in LPLD patients, including pancreatitis, are a consequence of chylomicron overload.”

## Product Pipeline

### Glybera

#### **Glybera® on Track for a Regulatory Decision by Mid-2011**

The key focus of AMT's activities during 2010 was to advance its lead product Glybera® (research code name AMT-011, non-proprietary name alipogene tiparvovec) towards market approval. Following the initial filing of Glybera® with the European Medicines Agency (EMA) on December 23, 2009 the EMA conducted its initial review of the Glybera® registration dossier during the first half of 2010 and sent the Day 120 List of Questions to AMT in May 2010. In July, the Company had two meetings with the Committee for Advanced Therapies (CAT) at the EMA for clarification about those questions which enabled AMT to finalize its strategy for responding to these questions in a timely and effective manner. The outcome of the meetings suggests that AMT will not be required to conduct more clinical trials with additional new patients at this time. The response to the questions was based in part on additional data and analyses from patients previously treated with Glybera®, including new data available from the last clinical trial and its one-year extension, and submitted to the EMA in November 2010. The EMA restarted evaluation on November 26, 2010, which represents Day 121. AMT has received, at Day 180, a significantly reduced list of outstanding items. The Company is now in the process of compiling the responses and expects to submit answers to the EMA by end of the first quarter. Based on the progress achieved with the EMA to date and the strong data package AMT remains confident that Glybera® continues to be on track for a positive regulatory opinion in mid 2011.

AMT has the option whether to commercialize Glybera® itself or to partner in Europe, Canada, the US and/or elsewhere.

AMT will also seek permission to market Glybera® in Canada and, later, in the US. Filing in Canada is anticipated mid 2011.

## Other Core Programs: Strong Focus on Orphan Diseases in Areas of Unmet Medical Needs

### 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 Factor IX 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. However, protein replacement therapy is costly, cumbersome, and does not completely prevent bleeding. Administered once, AMT's hemophilia B gene therapy is aiming at restoring the function of blood clotting long-term and at a higher efficacy through the introduction of the functional gene for the Factor IX protein into the patients' liver cells. It is therefore expected to be perceived as a significant advance over the current regular dosing of recombinant Factor IX protein.

### Development Status and Partnering

First patients have been dosed in a Phase I/II exploratory clinical trial conducted and sponsored by St Jude Children's Research Hospital and UCL hospital to assess the safety and efficacy of different doses of hemophilia B gene therapy. Initial data demonstrate encouraging results both in terms of clinical benefit based on long-term expression and product safety. AMT will build on the outcome of this exploratory trial, and is preparing for additional clinical development work to establish safety, tolerability and proof-of-concept with a Factor IX gene therapy produced using AMT's proprietary, clinically validated production system. To that end, in 2010, AMT and its co-development partner St Jude Children's Research Hospital have successfully transferred Factor IX to AMT's manufacturing platform and demonstrated Factor IX in rodents. AMT has the exclusive commercialization rights to the factor IX gene used in the St. Jude trial. This gene therapy has a huge market and partnering potential as it could replace Factor IX replacement entirely. AMT intends to partner it in the short- to mid-term.

### Duchenne Muscular Dystrophy (DMD)

Is a severe orphan disease characterized by progressive muscle degeneration. It affects young children, almost exclusively boys. The disease is caused by mutations in the dystrophin gene, which is located on the X-chromosome, thereby blocking 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 muscles that control breathing no longer function adequately. Currently there is no cure available and patients die in young adulthood. Innovative gene therapy approaches provide a big promise of preventing this fatal disease outcome with a single treatment. AMT is developing a gene therapy product based on 'exon skipping' technology which effectively bypasses the genetic defect so that a functional dystrophin protein can be produced.

## Product Pipeline

### Other Core Programs

#### Development Status and Partnering

AMT has shown life long therapeutic efficacy of its gene therapy treatment AMT-080 in studies of a preclinical rodent model of DMD. These studies were performed in collaboration with the Prof. Bozzoni's group at the University of Rome. The proof-of-concept studies demonstrated that AMT's technology resulted in functional dystrophin synthesis in both heart and skeletal muscles, leading to the prevention of muscular dystrophy. These data are strengthened by a study in which this gene therapy approach was shown to successfully restore dystrophin activity in diseased human muscle cells obtained from biopsies of DMD patients. In 2010, AMT made significant progress in further developing and optimizing the technique for delivery to heart muscles in different species. These 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. A Phase I/II clinical trial is scheduled to start in 2013.

AMT intends to commercialize the project itself, but is also flexible to work with suitable partners.

#### Acute Intermittent Porphyria (AIP)

Is a rare liver metabolic disorder resulting from mutations in the PBDG gene, which encodes for the enzyme uroporphobilinogen 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 attacks, 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 their full consequences. AMT-021 is intended to provide long-term normalization of the PBGD protein in order to prevent acute attacks and their complications.

#### Development Status and Partnering

AMT has demonstrated that its product AMT-021 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. AMT's partner at the Centro de Investigación Médica Aplicada (CIMA) has shown persistence of expression of genes in the liver for more than a year, using AAV-mediated delivery methods similar to AMT-021. During 2010, AMT has produced the material necessary for pivotal preclinical toxicology studies that are required for the approval for initial clinical development. AMT's partner CIMA anticipates starting those studies in March 2011, and patient enrolment in an interventional clinical trial is expected to begin in 2012. In January 2011, the EU finalized a €3.3 million grant to the AIPGENE consortium, of which AMT is a member, for the development a gene therapy product for AIP. Of this grant AMT

will receive €1.1 million. It will cover approximately 75% of AMT's overall development costs to bring AMT-021 forward to completion of a Phase I/II study in humans. AMT intends to market the product itself.

### **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 or eventually impossible. The symptoms are caused by degeneration and death of nerve cells in the specific part of the brain that produces dopamine, a chemical which sends messages in the brain to control movement. At present, there is no cure for PD, but medications or surgery can provide relief from the symptoms. The most widely used form of treatment is still 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 (glial cell derived neurotrophic factor) protein into the brain is effective in PD. GDNF stimulates the formation of dopamine and prevents further degeneration of dopaminergic neurons. AMT's aim is to inject recombinant AAVs (see page 105) that carry the gene for GDNF into the brain.

### **Development Status and Partnering**

Together with the University of Lund, Sweden, AMT is working on the preclinical development of a gene therapy, 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. Efficacy data in an animal model of PD is anticipated to be available in the first half of 2011. Previous studies using intracerebral injections of GDNF protein as well as gene therapy approaches in animal models have shown that GDNF can effectively protect injured dopamine-producing neurons and stimulate dopamine turnover and release. Based on promising early results of this approach, AMT believes there is an opportunity for a similar approach in a range of CNS disorders with the aim to protect and enhance the function of affected nerve cells. To this end, AMT has renegotiated its agreement with Amgen that now allows AMT to progress the GDNF program also in alternative gene therapy applications such as Huntington's disease or Multiple System Atrophy (MSA). The plan is to start clinical development in 2012.

### **Sanfilippo**

Is a rare autosomal recessive lysosomal storage disease, which manifests in young children and leads to progressive neuronal degeneration and death. Initial symptoms include a slowing of development and/or behavioral problems, followed by progressive intellectual decline resulting in severe dementia and progressive motor disease. In the final phase of the illness, children become increasingly immobile and unresponsive, often require wheelchairs, and develop swallowing difficulties and seizures. The life-span of an affected child does not usually extend beyond late teens to early twenties. Currently there is no approved therapy for this disease.

## Product Pipeline

### Other Core Programs

## Development Status and Partnering

Early 2011, AMT entered into an agreement with Institut Pasteur and a group of French research institutes (together the “Consortium”) to support clinical development of a novel gene therapy to treat Sanfilippo B. On behalf of the Consortium, Institut Pasteur will lead the development program and will also sponsor the initial Phase I/II clinical study of a gene therapy to replace an enzyme (alpha-N-acetylglucosaminidase) that is missing in brain cells of Sanfilippo B patients. AMT will manufacture and supply the adeno-associated viral (AAV5) gene therapy product to the Consortium, leveraging AMT’s proven expertise in cGMP manufacturing of gene therapy products and its experience in progressing these products through clinical development and the regulatory processes needed for successful commercialization. The French Muscular Dystrophy Association (AFM), a Consortium member, will fully fund the development program through to completion of the Phase I/II clinical study, including all AMT manufacturing costs. If the Consortium successfully demonstrates proof of concept in the Phase I/II study, AMT will have an option to acquire full commercial rights for the program. The Phase I/II clinical study is scheduled to begin before 2013.

In December 2010, Consortium researchers published preclinical data on the Sanfilippo B gene therapy. This data demonstrated safety and efficient spreading of the AAV5 gene vector particles throughout the brain in models of the disease. The gene vectors also exhibited long-term viability within the cells and an improvement of histological and biochemical markers.

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# Corporate Governance Report

This report is the corporate governance statement as defined in Section 2a of the Decree of December 23, 2004 (most recently amended on December 10, 2009) for the adoption of further regulations governing the contents of the annual report ('the Decree').

## Shares and Shareholders Rights

For details on the number of outstanding shares, see Note 9 ("Shareholders' equity") to the financial statements included in this Annual Report.

## Issuance of Shares, Pre-emptive Rights and Acquisition of Own Shares

On April 28, 2010 the Annual General Meeting of Shareholders extended the period of its delegation of the authority to issue shares or grant rights to subscribe for shares, to the Management Board for a period ending on October 28, 2011. Any resolution by the Management Board to issue shares or grant rights to subscribe for shares, is subject to the approval of the Supervisory Board. Such authority may be further extended, either by an amendment to the Articles of Association, or by a resolution of the General Meeting of Shareholders, for a subsequent period of up to five years in each case. A subsequent delegation pursuant to a resolution of the General Meeting of Shareholders shall require a proposal by the Management Board, which in its turn requires the approval of the Supervisory Board.

The above-mentioned delegation to the Management Board includes all shares in the authorized capital of the Company, as it stands from time to time. The increase of the authorized capital, which was resolved upon by the General Meeting of Shareholders in its extraordinary meeting of September 20, 2010, consequently increased the authority of the Management Board under this delegation accordingly.

Following termination of the Management Board's authority to issue shares or grant rights to subscribe for shares, the General Meeting of Shareholders shall be authorized to do so, unless it delegates this authority to the Management Board or to the Supervisory Board. A resolution of the General Meeting of Shareholders to issue shares or grant rights thereto shall require a proposal by the Management Board, which in its turn requires the approval of the Supervisory Board.

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



## **Pre-emptive Rights**

Dutch law and the Articles of Association give 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 the Company's employees; and (iii) shares issued to persons exercising a previously granted right to subscribe for shares.

On April 28, 2010 the Annual General Meeting of Shareholders also extended the period of its delegation of the authority to limit or exclude pre-emptive rights in relation to an issue of shares to the Management Board for a period ending on October 28, 2011. A resolution of the Management Board to limit or exclude pre-emptive rights is subject to the approval of the Supervisory Board.

## **Acquisition of Own Shares**

The Company may acquire its own fully paid shares at any time for nil consideration (om niet). Furthermore, subject to certain provisions of Dutch law and the Articles of Association, the Company may acquire fully paid shares in the Company's own capital, within the limits set by Dutch law.

Unless for nil consideration, shares may only be acquired subject to a resolution of the Management Board, which is approved by the Supervisory Board, and authorized by the General Meeting of Shareholders. Such authorization from the General Meeting of Shareholders for the acquisition of the Company's 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. On April 28, 2010, the General Meeting of Shareholders furthermore extended its authorization to the Management Board to acquire a maximum of ten percent of the Company's issued ordinary shares for a period ending on October 28, 2011 at either: (i) a maximum purchase price of 110% of the weighted average closing price of the Company's ordinary shares in the last ten trading days; or (ii) the nominal value of the shares.

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. Any shares the Company holds in its own capital may not be voted or counted for voting quorum purposes.

### **Reduction of Share Capital**

Upon a proposal of the Management Board, subject to the approval of the Supervisory Board and to Dutch law, the General Meeting of Shareholders may resolve to reduce the Company's issued and outstanding share capital by canceling its shares, or by amending the Articles of Association to reduce the nominal value of the shares.

### **Dividends and Other Distributions**

The Management Board may, subject to the approval of the Supervisory Board, determine which part of the profits shall be reserved. The part of the profit remaining after reservation shall be distributed as a dividend on the shares.

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

The General Meeting of Shareholders may, at the proposal of the Management Board, 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 the Company's shares entitles its holder to equal ranking rights to dividends and other distributions.

### **General Meetings of Shareholders and Voting Rights**

The annual General Meeting of Shareholders shall be held within six months after the end of each financial year. The Company's financial year is equal to a calendar year.

An Extraordinary General Meeting of Shareholders may be convened, whenever the Company's interests so require, by the Management Board or the Supervisory Board. Shareholders representing alone or in aggregate at least one-tenth of the Company's issued and outstanding share capital may, pursuant to the Dutch Civil Code and the Articles of Association and after first requesting the Company to convene such a meeting, request a court for authorization to convene a General Meeting of Shareholders be convened, subject to the relevant provisions of Dutch law.

A record date shall apply, to establish which shareholders are entitled to attend and vote in the General Meeting of Shareholders. Such record date has been set by the Dutch Civil Code on the twenty-eight day before that of the meeting.

Each of AMT's shares is entitled to one vote. Shareholders may vote by proxy. The voting rights attached to any of the shares held by the Company are suspended as long as they are held in treasury.

Decisions of the General Meeting of Shareholders are taken by an absolute majority of votes cast, except where Dutch law provides for a qualified majority.

### **Amendment of the Articles of Association**

The General Meeting of Shareholders may resolve to amend the Articles of Association at the proposal of the Management Board which has been approved by the Supervisory Board.

### **Non Compliance with the Corporate Governance Code**

AMT acknowledges the importance of good corporate governance. The Management Board and Supervisory Board have reviewed the Corporate Governance Code (as restated on December 10, 2009). The full Dutch text of the Corporate Governance Code can be found at [www.commissiecorporategovernance.nl](http://www.commissiecorporategovernance.nl).

Corporate governance concerns the relationship between the various governing bodies of the Company: the Management Board, the Supervisory Board and the General Shareholders Meeting, as well as the other stakeholders of the Company. In particular it regulates the manner in which the Company is governed, the accountability of management and the supervision thereof. As a Dutch listed company, AMT is obliged to clarify in its annual report the extent to which it complies with the regulations and the best practices provision of the Netherlands' Corporate Governance Code in so far as they affect the Management Board and the Supervisory Board. If a company that is subject to the Netherlands' Corporate Governance Code does not, or does not intend to, comply with any of the principles or best practice provisions, it must explain its motivation thereto in its annual report. AMT subscribes to the principles and best practice provisions of the Corporate Governance Code. In this section AMT outlines how it has organized its corporate governance and to what extent it does not comply with the most relevant best practices of the Corporate Governance Code.

AMT supports the Corporate Governance Code and applies with the relevant best practice provisions of the Code, subject to the exceptions set out below.

III.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.

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AMT believes that to be able to attract the best qualified candidates available for its Management Board, it must be able to offer the best conditions available to it. It furthermore believes that this provision and the uncertainty entailed thereby would limit AMT's 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 (clawback clause).

AMT believes that compliance with this provision would also limit its abilities to attract the best qualified candidates available for its Management Board.

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.

The current Supervisory Board profile of AMT, as established at the initial public offering of AMT and published on AMT's website, was adopted under and in compliance with the previously prevailing Corporate Governance Code. This profile has not been aligned with the more detailed requirements of this provision under the currently prevailing Corporate Governance Code. The Supervisory Board believes that it is currently properly composed to perform its duties and that the Supervisory Board profile serves the general aim of this best practice provision properly. The Supervisory Board is in the process of updating its profile and anticipates that such update shall be completed in 2011. III.3.6 The supervisory board shall draw up a retirement schedule in order to avoid, as far as possible, a situation in which many supervisory board members retire at the same time. The retirement schedule shall be made generally available and shall be posted on the company's website.

The Supervisory Board believes that due to the changes in its composition in 2010, the retirement schedule of its current members, resulting from the variation in their dates of appointment, is such that continuity is ensured and that consequently, it does not require this to be detailed in a separate roster.

III.4.1 The chairman of the supervisory board shall ensure that ...  
f) the supervisory board elects a vice-chairman;

The size of the Company's Supervisory Board and the committed participation of the Supervisory Board members has meant that there has been no requirement for a vice-chairman. The company and the Supervisory Board continue to review this situation and will, if deemed appropriate, appoint a vice-chairman on such occasion as the Supervisory Board deems appropriate.

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 organisation of the affairs of the supervisory board (information, agenda, evaluation, training programme, 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 the small size of the Company. However, a substantial proportion of the role has been delegated to the company's legal advisers, who provide external advice and services.

III.4.4 The vice-chairman of the supervisory board shall deputise 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.

Reference is made to the explanation given in relation to best practice provision III.4.1.

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;

AMT feels that its financial reporting will be sufficiently monitored by its 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.

AMT considers 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, 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 AMT believes he is currently the best qualified person available.

III.5.11 The remuneration committee shall not be chaired by the chairman of the supervisory board or by a former member of the management board of the company, or by a supervisory board member who is a member of the management board of another listed company.

AMT considers the position of chairman of the remuneration and nominating committee to be of such importance that it should at all times be designated to the best qualified person available, even if such designation would not be in line with this best practice provision. Mr. Verdonck was chairman of both the Supervisory Board and the remuneration and nominating committee for the period to September 20, 2010 as AMT believed he was the best qualified person available during that time. Mr. Verdonck was replaced as Chairman of the remuneration and nominating committee by Mr. Steve Holtzman. Following the resignation of Mr. Holtzman after the year end, Mr. Verdonck has temporarily resumed chairing this Committee ad interim. The Supervisory Board will nominate a new chairman of this committee in the near future.

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.

AMT believes that the restrictions under Dutch securities law are sufficient to govern the ownership of and transactions in securities by members of the Management Board or by members of the Supervisory Board. Implementing additional restrictions would potentially harm the Company’s ability to attract and ensure the continued services of the members of the Management Board and of the Supervisory Board and the Company therefore believes that applying the final sentence of this best practice provision is not in its best interest.

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

AMT granted shares to the chairman and the members of the Supervisory Board. AMT believes that this is international common practice and may in future be further required to commit itself to grant options to attract and ensure the continued services of the best qualified persons for the Supervisory Board. AMT 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.

The Company is not permitted by law to pay dividends because it has no retained profits on account of its history of making losses. However in order to comply with this requirement in the future, the Company will table dividend and reserve policy as a separate item at a General Meeting of Shareholders in the 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 website and by means of press releases. Provision shall be made for all shareholders to follow these meetings and presentations in real time, for example by means of web casting or telephone lines. After the meetings, the presentations shall be posted on the company's website.

Considering AMT's 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. AMT does provide facilities for shareholders to follow the announcement of half-year and full year results via webcast. AMT also ensures 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 shall not take place shortly before the publication of the regular financial information (quarterly, half-yearly or annual reports).

The Company maintains an active program of meetings with investors, which it considers to be in the best interests of the Company and its 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. The Company's substantial research and development activities mean that it has a history of making losses and the Company believes that presently the main driver of price sensitive information are the progress that it makes on its 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.

The company is small and does not believe it is appropriate at this time to appoint an independent third party to hold proxies. The company does 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.

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The Company has not historically felt the requirement for such a policy and therefore did not comply. The Supervisory Board and Management Board 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.

Reference is made to the explanation given in relation to best practice provision II.5.4.



# Supervisory Board Members

## **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, KBC and earlier with Lazard Frères) and also in manufacturing (Bekaert N.V.). Currently, he is a director of Galapagos N.V. (Mechelen, Belgium), J. P. Morgan European Investment Trust (London), Groupe SNEF (Marseille), Laco Information Services (Diegem, Belgium) and Virtus Funds (Hartford, CT). Earlier he served as chairman of Banco Urquijo (Madrid) and director of Dictaphone Corporation (Stratford, CT) among other companies. Mr. Verdonck is a member of the General Council of the Vlerick Leuven Ghent Management School.

Nationality: Belgian. Age: 68



## **Philippe Van Holle – Member**

Mr. Van Holle is Head of Celgene Europe. He 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 two first 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.

Nationality: Belgian. Age: 55



## **Sander van Deventer – Member**

Professor van Deventer, one of AMT's co-founders, holds a degree in Medicine as well as a PhD from the University of Amsterdam. He was Professor and Head of the Department of Experimental Medicine, Chairman at the Department of Gastroenterology of the AMC from 2002 to 2004, and subsequently Professor of Experimental Medicine at the University of Amsterdam Medical School until 2008. He is the author of more than 350 scientific articles in peer-reviewed journals, and he serves as an advisor to regulatory authorities including the EMA and FDA. Currently, he is Professor of Translational Gastroenterology at the Leiden University Medical Center (LUMC) and a partner of Forbion Capital Partners. Sander van Deventer serves on the boards of Cardoz AS, based in Stockholm, Sweden, and Argos Biotherapeutics, Durham NC, USA.

Nationality: Dutch. Age: 56



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### Supervisory Board Members



#### **Joseph M. Feczko, M.D.**

Dr. Feczko was formerly 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. He is Chairman of Cardoz Pharmaceuticals AB (Sweden) and a Director of Keryx Biopharmaceuticals, Inc. (US), as well as a member of the Board of Directors of the Foundation for the National Institutes of Health, the International Longevity Center, and the New York Academy of Medicine (all US). 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.

Nationality: US. Age: 61



#### **François Meyer**

Dr. Meyer was formerly General Director for Research and Development at RPR and then Aventis Pharma, France until 2002 and Director-General of Aventis' Gene Therapy Division, Gencell until his retirement in 2006. He is a Director of BioSeek, Inc. (US), Urogene SA (France), Introgen Therapeutics, Inc. (US) and Gene Therapy, Inc. (US), and a Member of the Scientific Advisory Boards of Genethon (France), Systemix, Inc. (US) and Biotransplant, Inc. (US).

Nationality: Luxembourg. Age: 62

# Report of the Supervisory Board

## Financial Statements

We are pleased to present the annual report and financial statements for 2010 as prepared by the Management Board. The financial statements have been audited by PricewaterhouseCoopers Accountants N.V.. The auditor's report endorsing the financial statements can be found on page 100 of this report. The Supervisory Board discussed the annual report with the Management Board in the presence of the auditor. The discussion and input from the parties present at the meeting allow us to state with confidence that the annual report satisfies the transparency requirements and provides a good basis for the Supervisory Board's accountability for the supervision it conducted. The Supervisory Board recommends that you adopt the annual report, and discharge the members of the Management Board and Supervisory Board for the policy they have pursued and their supervision in the past financial year.

The financial statements for 2010 for Amsterdam Molecular Therapeutics (AMT) Holding N.V. have been prepared in accordance with International Financial Reporting Standards as adopted by the European Union and, in our opinion, give a true and fair view of the Group's and the Company's assets, liabilities, financial position and results at December 31, 2010 and of the results of the Group's and the Company's operations and cash flows for the financial year 2010.

## Results

During the year under review AMT continued to build on its future and made solid progress with its clinical development and research projects. It has been another significant year. Glybera®'s progression through the European registration process is a major exercise, which has continued to absorb considerable resources. Glybera® could be the first gene therapy product to treat a genetic disease to be approved for sale in Europe.

AMT's second gene therapy product has now entered development for Hemophilia B. The study is being led by St Jude Children's Research Hospital and UCL Hospital. Initial data presented at the American Society of Hematology (ASH) conference in Florida in December 2010 showed that dose-dependant, safe, stable and persistent expression in patients has been observed. Because AMT's technology can be applied equally to a wide range of other genetic diseases, the success of Glybera® would validate AMT's approach for its other pipeline products, targeting a range of orphan and major diseases, including Parkinson's Disease, DMD and AIP.

In October 2010, AMT successfully raised €14.3 million of new funds before expenses (€13.3 million net of costs) via a private placement of ordinary shares. These funds, together with our existing cash resources, take AMT comfortably through the assessment process of Glybera®. The Company also expects to generate significant additional revenue from commercialising Glybera® and from developing its collaborations with other parties. Taking these additional funding sources into account, AMT believes it will have sufficient cash resources to meet its operational requirements.

## Financial Report

### Report of the Supervisory Board

The Supervisory Board wishes to take this opportunity to express to all employees a sincere appreciation for their efforts and commitment, which contributed to the further development and growth of AMT in the past year.

## Supervision and Advice

### Activities, Policy, Strategy, Realization

During the year under review, the Supervisory Board held extensive discussions, both in its formal meetings, and also in informal communications among its members, to ensure the continuity of high level management of the Company. The Supervisory Board held 6 formal meetings for consultation with the Management Board. During these formal meetings and discussions, the Supervisory Board primarily focused on the objectives and strategy of AMT, and the main risks of its business, the assessment made by the Management Board of the design and effectiveness of the internal risk management and control systems, the progress made on clinical development, corporate governance, the financial budgets and operational plan, the half yearly report and progress on fulfilling the proposed plans. The Supervisory Board discussed clinical development and strategy at length with the Management Board in terms of the developments in its particular field of expertise, gene therapy. In the same context, the Supervisory Board also discussed the long-term plan that ties in with the aspiration, objectives, and strategy. Special attention was devoted to the realism of the assumptions made, maintaining a manageable risk profile and the Company's financing and staffing plan. Based on these assumptions, the proposed strategy should allow for growth in the value of the share. The Supervisory Board extensively discussed the situation in the biotechnology industry, research and clinical developments, acquisition opportunities, possible cooperation with third parties and the staffing plan of AMT. The discussion of the realization of the proposed plans centered mainly on progress in development of various pipeline products, collaboration with academic and industrial partners, reasons why the progress of some development programs lagged, and the measures taken in response. There was also regular consultation on the modernization of the infrastructure, investment in operating assets and the availability of sufficient high quality managers.

### Corporate Governance

The Board wishes to draw attention to AMT's compliance with the majority of the provisions in the prevailing Corporate Governance Code. Details of AMT's position regarding the organization of the corporate governance structure is presented starting on page 22 of this report. This subject will be included in the agenda of the Annual General Meeting of Shareholders.

The Corporate Governance Code stipulates that the composition of the Supervisory Board is such that it is able to carry out its duties properly and that the members of the Supervisory Board are able to act critically and independently of each other, of the Management Board and of any particular interests.

In 2010 the composition of the Supervisory Board and their attendance at Supervisory Board meetings was as follows:

	Eligible	Attended
Ferdinand Verdonck (Chairman)	6	6
Philippe van Holle	6	6
Sander van Deventer <sup>1</sup>	4	4
Joseph Feczko <sup>2</sup>	2	2
François Meyer <sup>2</sup>	2	2
Steven Holtzman <sup>2,3</sup>	2	2
Alexander Ribbink <sup>4</sup>	3	2
George Morstyn <sup>5</sup>	3	1

<sup>1</sup> Appointed April 28, 2010

<sup>2</sup> Appointed September 20, 2010

<sup>3</sup> Resigned January 3, 2011

<sup>4</sup> Resigned April 28, 2010

<sup>5</sup> Resigned June 30, 2010

The appointments of Mr. Verdonck and Mr. van Holle run to the date of the first General Meeting of Shareholders following April 16, 2012, when they shall both be eligible for re-election. Professor van Deventer's appointment runs to the date of the first General Meeting of Shareholders following April 28, 2014, when he shall be eligible for re-election. The appointments of Dr. Feczko and Mr. Meyer run to the date of the first General Meeting of Shareholders following September 20, 2014, when each of them shall be eligible for re-election.

### Functioning of the Supervisory Board

The members of the Supervisory Board have discussed their individual functioning, as well as that of the Supervisory Board as a whole, on a continuing basis. In these discussions, also consideration was given to the composition and profile of the Supervisory Board, as well as the functioning of its members and committees and the Supervisory Board's tasks. The profile sets out the types of expertise the Supervisory Board must possess. In our view the Supervisory Board satisfies the defined requirements, and we consider the composition to be adequate for the proper performance of its duties. The Supervisory Board has appointed from among its members two separate committees with special tasks, the Audit Committee and the Nominating and Remuneration Committee. These committees prepare the decision making of the Supervisory Board on the relevant matters. The following Regulations can be found on the Company's website: Management Board Regulations, Supervisory Board Regulations, Audit Committee Regulations, and Remuneration and Nominating Committee Regulations.

## Financial Report

### Report of the Supervisory Board

#### Audit Committee

The Audit Committee mainly assists the Supervisory Board in its responsibilities for monitoring financing, financial statements, the financial reporting process and the systems of internal business controls and risk management.

In 2010, the Audit Committee was composed of Messrs. Verdonck (chairman), van Holle and (until his resignation) Ribbink. Upon his appointment to the Supervisory Board Professor van Deventer also became a member of the Audit Committee. The Audit Committee held 3 formal meetings, in which amongst others the following were discussed:

- the financial results for the fully year ended December 31, 2009, the half year results for the period ended June 30, 2010 and the full year results for the year ended December 31, 2010;
- the Company's system of internal controls; and
- the external audit approach, planning and results.

#### Remuneration and Nominating Committee

The Remuneration and Nominating Committee in particular makes recommendations regarding the remuneration policy for the Management Board to be adopted by the General Meeting of Shareholders, prepares proposals to the Supervisory Board for remuneration of individual members of the Management Board and advises the Supervisory Board in the level and structure of compensation for other senior personnel.

Furthermore, the Remuneration and Nominating Committee makes recommendations to the Supervisory Board regarding candidates for service on the Management Board and the Supervisory Board.

In 2010 the Remuneration and Nominating Committee was composed of Messrs. Verdonck (Chairman) and Morstyn (until his resignation). Upon their appointments as members of the Supervisory Board, Dr. Fezcko, Mr. Meyer and Mr. Holtzman became members of the Remuneration and Nominating Committee; Mr. Verdonck stood down from the Committee and Mr. Holtzman was appointed Chairman of the Committee. On Mr. Holtzman's resignation from the Supervisory Board, Mr. Verdonck resumed the Chairmanship of the Committee.

The Remuneration and Nominating Committee held 2 formal meetings, each of which was held as part of a full Supervisory Board meeting. Furthermore, in preparation for these meetings and in the light of the Company's search for continuity of high level management, the members of the Remuneration and Nominating Committee had extensive bi-lateral discussions outside of formal meetings. In these meetings and discussions the following main topics were discussed:

- the composition and functioning of the Supervisory Board and the Management Board, the goals for the Management Board, and the actual performance of the Management Board compared to the goals;
- the remuneration of the Management Board and staff members.

The Company's Remuneration policy was approved at the Annual General Meeting of Shareholders that was held on April 15, 2009 and amended at the Annual and Extraordinary General Meetings of Shareholders that were held on April 28, 2011 and September 20, 2010. The policy, as well as the composition of the remuneration package and size of the individual components of individual Management Board members, are compared periodically with market developments. This includes comparing the package with the remuneration of management boards of listed companies similar in size to AMT. The Remunerating and Nomination Committee decided that a management bonus would be issued regarding the financial year 2010, as described in the Notes to the Financial Statements. The Remuneration Report of the Supervisory Board, in accordance with section II.2.12 of the Corporate Governance Code is set out below.

The Corporate Governance Code stipulates that the composition of the Supervisory Board is such that it is able to carry out its duties properly and that the members of the Supervisory Board are able to act critically and independently of each other, of the Management Board and of any particular interests.

## **Remuneration Report**

This report sets out the remuneration policy operated by the Company in respect of the Management Board. Details of the members and meetings of the Remuneration and Nominating Committee are disclosed above.

## **Remuneration Policy Overview**

It is the aim of the Remuneration and Nominating Committee to encourage and reward superior performance by the members of the Management Board with that performance being measured against achieving corporate goals, strong financial performance and the delivery of value to shareholders.

## Financial Report

### Report of the Supervisory Board

The Remuneration and Nominating Committee believes that the current policy retains and motivates the Management Board appropriately while enforcing a strong “pay for performance” culture within the company. The Remuneration and Nominating Committee will continue to review the policy on an annual basis to ensure that it is in line with the company’s objectives and shareholders’ interests.

Details of amounts paid to the Management Board and to the senior management team of the company are set out in Note 23 to the Financial Statements.

### Management Board Agreements

The terms and conditions of Mr. Aldag’s service contract were approved by the Extraordinary General Meeting of shareholders held on November 4, 2009. The terms and conditions of Mr. Morgan’s service contract were approved by the Annual General Meeting of shareholders held on April 28, 2010. Messrs. Aldag and Morgan are the only members of the Management Board at the date of these accounts.

### Pensions

Within AMT’s pension scheme both employee and employer make contributions which are invested in investment funds selected by the employee. Every year a premium is made available by AMT, expressed as a percentage of the pensionable salary of the employee. The employee’s contribution amounts to 6.1% of pensionable salary and will be settled through deduction from the gross monthly salary. Each year on January 1st, the available premium will be automatically adjusted to the employees’ new gross salary. AMT’s contribution to the pension scheme is related to the age of the employee, on an increasing basis in the range 6.9–36.1% of pensionable salary for ages between 20 and 65. The scheme is open to the members of the Management Board and employees.

### Salary

Basic salaries are reviewed annually and revised salaries take effect from the start of the financial year. The review process is managed by the Remuneration and Nominating Committee which each year assesses the market competitiveness of pay primarily in terms of total remuneration, with less emphasis on base salary.

### Bonuses

The maximum achievable bonus for Messrs. Aldag and Morgan is determined under their respective contracts at 30%. The performance criteria determining the actual level of bonus payable are set by the Supervisory Board on the recommendation of the Remuneration and Nominating Committee, by reference to the achievement of the Company’s goals for the year.



## **Share Options**

The Company issues share options to members of the Management Board and staff to reward loyalty and performance and to enable valued employees to share in the success of the Company. These options are effected by the grant of share options under the Company's share option scheme or by Depositary Receipts which may be exchanged after a period of three years into an equivalent number of shares in the company.

## **Directors' Share Options**

Details of Directors' share options are set out in Note 23 to the Financial Statements.

## **Independence of the Supervisory Board**

Save for Professor van Deventer, who was a member of the Management Board prior to his appointment to the Supervisory Board, the Supervisory Board has been and remains fully independent within the meaning of best practice provision III.2.2 of the Dutch Corporate Governance Code.

Amsterdam, March 4, 2011  
Supervisory Board  
Ferdinand L. J. Verdonck – Chairman  
Philippe Van Holle – Member  
Sander van Deventer – Member  
Joseph Feczko – Member  
François Meyer – Member

## Key Members of the Management Team



### Jörn Aldag – CEO

Mr. Aldag joined AMT in October 2009 as Chief Executive Officer. He has over twenty five years experience of executive, business and financial management, at Evotec AG, MAN AG and Treuhandanstalt. Currently, he is Chairman of Molecular Partners AG in Switzerland, and Member of the Supervisory Board of the DESERTEC Foundation. He holds business degrees from Harvard Business School and the European Business School.



### Mark Chadwick – Patent Counsel

Dr. Chadwick joined AMT in November 2008 as Patent Counsel. He holds a degree in Natural Sciences from the University of Cambridge and a PhD in Genetics from the University of East Anglia. Before joining AMT, Mr. 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

Mrs. Marelis joined AMT in August 2008 as Director Human Resources. She holds an MBA from Kingston University in London. Prior to joining AMT, Mrs. Marelis worked at Dell, where she spent five years working as Manager Human Resources. Prior to joining Dell, Mrs. 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 AMT in August 2010 as Director Regulatory Affairs. She holds a PhD in Microbiology and Immunology from the University of Bonn. Prior to AMT Dr. Meyer was responsible for European Regulatory Affairs with Human Genome Sciences covering autoimmune, oncology and Hepatitis C products, and previously she spent three years with CSL Behring. She is also vice-chair of the BioManufacturing Working Group of the European Biopharmaceutical Enterprises.



### Piers Morgan – CFO

Mr. Morgan joined AMT in December 2009 as Chief Financial Officer. He has over 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.

### **Harald Petry – Director of Research and Development**

Dr. Petry joined AMT in May 2007 as Director of the 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 PhD he built up a career in academic research; for the last 10 years he has worked at Jenapharm GmbH (Germany), Berlex Biosciences (US) and AMT (The Netherlands) in different functions with increasing managerial and leadership responsibility.



### **Hans Preusting – Director Operations and Project Management**

Dr. Preusting joined AMT in August 2006 and is responsible for Operations and Project Management within AMT. Dr. Preusting holds a PhD in Biochemistry and has over 15 years of experience in manufacture using fermentation and cell culture techniques. Prior to AMT his roles included Solvay Pharmaceuticals and DSM. Dr. Preusting holds two patents and has published over 20 scientific articles.



### **Tamara Tugal – Business Development Director**

Dr. Tugal joined AMT in June 2008 and is responsible for business development. Dr. Tugal holds a BSc in Molecular Biology from the University of Edinburgh, a PhD in Biochemistry from University College London, and holds an MBA from London Business School. Prior to AMT, Dr. Tugal held business and managerial roles at Lorantis Ltd and at Eden Biodesign Ltd.



### **Arnold Vroege – Director Quality Assurance**

Mr. Vroege joined AMT in January 2007 as Director Quality Assurance and Quality Control. 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 subsequently 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.



### **Janneke de Wal, M.D – Director Global Marketing and Sales**

Dr. de Wal joined AMT in August 2008 as Director Global Marketing and Sales. She graduated in medicine from the University of Leiden Medical School (the Netherlands) with honors. Prior to AMT, Dr. de Wal spent five years with Genzyme, working in European and Global sales, including the marketing of Cerezyme. Before Genzyme, Dr. de Wal spent 17 years in the pharmaceutical industry, and has been responsible for the launch of products across a broad range of indications.



# Report of the Management Board

## General Information

Amsterdam Molecular Therapeutics (AMT) Holding N.V. is a public company with limited liability 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., a private company with limited liability. That name was subsequently changed into Amsterdam Molecular Therapeutics (AMT) Holding B.V., effective as of June 5, 2007. As of that date, the intellectual property activities and other activities (such as production and research & development) were transferred by means of a statutory demerger (afsplitsing) into two newly incorporated private companies with limited liability (besloten vennootschappen met beperkte aansprakelijkheid), named Amsterdam Molecular Therapeutics (AMT) IP B.V. and Amsterdam Molecular Therapeutics (AMT) B.V. These companies are both one hundred percent subsidiaries of Amsterdam Molecular Therapeutics (AMT) Holding N.V.

On June 20, 2007, the Company was converted into a public company with limited liability and its Articles of Association were amended to allow for its shares to be traded on Euronext exchange. When in this chapter a reference is made to Articles of Association, this shall be a reference to the Company's Articles of Association, as they read as of September 29, 2010. These Articles of Association are available on the Company's website.

## AMT's Governance

AMT has a so-called two-tier governance structure in which the executive and supervisory responsibilities are separated. The Management Board is responsible for the day-to-day affairs of the Company. The Supervisory Board supervises and provides advice to the Management Board. Certain decisions of the Management Board, as outlined in the Articles of Association, require the prior approval of the Supervisory Board. Furthermore, the Supervisory Board can inform the Management Board that additional decisions of the Management Board require prior approval of the Supervisory Board. In executing their supervisory role, the members of the Supervisory Board must be guided by the best interests of the Company and all its stakeholders. The Management Board as well as the Supervisory Board shall report to the Annual General Meeting of Shareholders with regard to AMT's corporate governance regarding its structure and compliance with the Corporate Governance Code.

## **Management Board**

The Management Board is responsible for the general affairs and business of the Company and as such is responsible for progressing the Company to achieve its goals.

During 2010 the following people were members of the Management Board:

- Jörn Aldag; Chief Executive Officer. Mr. Aldag joined the Company as Chief Executive Officer on October 5, 2009, and was appointed to the Management Board by the General Meeting of Shareholders held on November 4, 2009; and
- Piers J. Morgan; Chief Financial Officer. Mr. Morgan joined the Company as Chief Financial Officer on December 1, 2009, and was appointed to the Management Board by the Annual General Meeting of Shareholders held on April 28, 2010.

The Management Board has collective powers and responsibilities, which, if the Management Board is comprised of more than one member, are divided among its members. Any such division of these powers and responsibilities and the rules governing the Management Board's internal organization are laid down in Regulations. The General Meeting of Shareholders appoints members of the Management Board, based on the proposals of the Supervisory Board. A member of the Management Board shall be appointed for a period of four years and may be reappointed for additional periods of four years each.

## **Supervisory Board**

The Supervisory Board is responsible for supervising the conduct of and providing advice to the Management Board and supervising AMT's business generally. In performing its duties, the Supervisory Board is required to act in the interests of the Company's business as a whole, with due regard of the social responsibility issues connected therewith. The Articles of Association provide that the Supervisory Board will determine the number of members of the Supervisory Board and that the General Meeting of Shareholders appoints the members of the Supervisory Board following a proposal by the Supervisory Board.

Any newly appointed member of the Supervisory Board will serve for a maximum of four years, unless stated otherwise in the resolution to appoint the Supervisory Board member in question. A Supervisory Board member may only be reappointed twice. The General Meeting of Shareholders appoints a chairperson and the Supervisory Board may appoint a vice-chairperson from amongst its members.

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

## Financial Report

Report of the Management  
Board

## Summary of the Full Year Results

### Key Highlights

- Glybera® Marketing Authorisation Application remains on track with European Medicines Agency (EMA);
  - Responses to Day 120 questions submitted in November 2010;
  - Day 180 list of Outstanding Issues now received;
- Raised €14.3 million through private placement;
- Novel biomarker for Glybera® activity identified;
- Diagnostic gene chip for LPLD developed by AMT's collaborator, Progenika, obtained CE Mark;
- Hemophilia Phase I/II study underway, being led by St Jude Children's Hospital and UCL Hospital; data from initial patients showed safe, stable expression;
- DMD program progressing with US Orphan Drug Status granted and up to €4 million Senter Novem funding;
- Porphyria program funding through EU grant now finalized;
- GDNF program progressing following renegotiation of collaboration agreement with Amgen; and
- New collaboration initiated with consortium led by Institut Pasteur to develop SanfilippoB gene therapy.

## Operations

### Lipoprotein Lipase Deficiency (LPLD)

The advance of AMT's lead product, Glybera® towards market approval was the key focus of the Group's activities during 2010. The regulatory process continues to progress on schedule. Following the filing of Glybera® with the European Medicines Agency (EMA) as a treatment for lipoprotein lipase deficiency (LPLD), the agency conducted its initial review of the Glybera® registration dossier in early 2010 and sent the Day 120 List of Questions to AMT in May. AMT submitted its response to the EMA in November 2010, based in part on additional data and analyses from patients previously treated with Glybera®, including new data available from the last clinical trial and its one-year extension. The EMA restarted evaluation on November 26 (Day 121), and following the normal centralized review procedure, AMT has received, at Day 180, a significantly reduced list of outstanding items. We are now in the process of compiling the responses and expect to submit answers to the EMA by end of the first quarter and believe to be on track for a mid 2011 response on marketing approval.

Because AMT's technology can be applied equally to a wide range of other genetic diseases, the success of Glybera® would validate AMT's approach for its other pipeline products, targeting a range of orphan diseases and diseases with large patient populations, in each case where there is high unmet medical need, including Parkinson's disease, hemophilia, Duchenne muscular dystrophy (DMD) and acute intermittent porphyria (AIP).

## **Hemophilia B**

The hemophilia B program has entered a Phase I/II clinical study, led by our partners St Jude Children's Research Hospital, Memphis, Tennessee, and University College London (UCL) Hospital, London, UK. Initial data presented at the American Society of Hematology (ASH) conference in Florida in December 2010 showed that dose-dependent, safe, stable, and persistent expression in patients has been observed.

## **Porphyria**

Our collaboration with FIMA in Pamplona, Spain, to develop a gene therapy for acute intermittent porphyria (AIP) is progressing very well, and has generated positive pre-clinical data. The program is now entering toxicology studies and a Phase I/II study is scheduled to begin in early 2012. Total grant funding of €3.3 million for this project has been secured from the EU, with €1.1 million assigned to AMT, supporting our financial commitment to this project.

## **Duchenne Muscular Dystrophy**

The DMD program continues to progress, with up to €4 million of financial support from Senter Novem, which covers 35% of development costs through to completion of the Phase I/II study. In September 2010, the US FDA granted our gene therapy for DMD Orphan Drug status. This complements the Orphan Drug status granted to the same program by the EMA covering Europe in 2009.

## **GDNF**

AMT has successfully renegotiated the terms of its collaborative agreement with Amgen covering the use of GDNF in gene therapies. AMT now has the ability to explore development of additional indications, including orphan diseases, alongside the development of Parkinson's disease. The University of Lund, Sweden, is performing preclinical studies in Parkinson's disease models for this program, the results of which are encouraging.

## **SanfilippoB**

Immediately after the year-end, AMT announced a collaboration with Institut Pasteur and the Association Française contre les Myopathies (AFM) to develop a gene therapy for the rare lysosomal disorder, Sanfilippo B for which Institut Pasteur has achieved preclinical proof of concept. Under the agreement, AMT will receive funding to manufacture the product using its AAV vector technology to progress the program through a Phase I/II study. Thereafter, AMT will have an option to acquire full commercial rights to the program.



## Financial Report

Report of the Management  
Board

### Financing

To fund Glybera® further through its regulatory and commercial development and to continue the development of the hemophilia B and other pipeline programs, AMT increased its financial flexibility significantly during the year. On October 6, 2010 AMT successfully raised €14.3 million through the sale of 8.4 million new ordinary shares at €1.70 each. Investors included key shareholders Advent Venture Partners, Crédit Agricole Private Equity, Forbion Capital Partners and Gilde Healthcare Partners, plus AMT management. In addition, AMT received an innovation credit of €4 million from the Dutch government's Innovation Agency, in January 2010, for the development of its DMD treatment. The credit will fund 35% of all the development costs of this project through mid 2013. The loan is repayable only if AMT successfully commercializes the product. In January 2011 AMT announced the finalization of an EU grant to fund €1.1 million of AMT's costs towards the Prophyria program, equivalent to 75% of the costs to complete a Phase I/II clinical study.

### Results

#### Revenues

The total net income for the year ended December 31, 2010 amounted to €1.4 million, a €1.0 million increase compared to the total net income for the year ended December 31, 2009, which amounted to €0.4 million. These revenues represent grant income from the Dutch government and the European Union.

#### Operating Costs

Research and development expenditure totaled €16.4 million, compared to €13.2 million in 2009, an increase of €3.2 million reflecting the ongoing level of activity to support the filing of Glybera, as well as ongoing development on AMT's other projects, including the Duchenne program (which is partly funded by the investment credit from Senter Novem) and reflecting the activities financed by the grants described above. In addition, research and development expenditure in 2010 included the €0.5 million of impairment charges and the largest part of the €0.5 million increase in charges relating to share-based incentive schemes, both of which represent non-cash items.

General and administrative costs decreased to €4.1 million, from €4.9 million in 2009. This decrease reflected the lower level of advisory costs in 2010, compared to 2009, as well as the fact that 2009 contained certain reorganization costs.

#### Operating Result

AMT's operating loss rose to €19.1 million for 2010, from €17.8 million for 2009, an increase of €1.3 million. This increase can be largely accounted for by certain non-cash items amounting to €1.0 million, comprising an increase of €0.5 million



in charges relating to share-based incentive schemes, a €0.3 million charge relating to impairment charges on certain intangible assets following the termination of a 2008 collaboration agreement, and a €0.2 million charge in respect of the impairment of certain leasehold improvements. After excluding for these non-cash, non-recurring items, the operating loss in 2010 would have been broadly equivalent to the operating loss for 2009.

### **Finance Income and Costs**

Net finance income fell to €0.5 million compared to €0.6 million in 2009, reflecting the lower average cash balances of the Group during 2010 during a period when interest rates available on cash deposits remained low. In addition, finance costs increased to €0.5 million (2009: €0.0 million). Finance costs in 2010 comprised interest of €0.3 million on the 2009 convertible bond, together with a non-cash charge of €0.2 million relating to the revaluation of foreign exchange transactions on currency accounts.

### **Result for the Year and Loss per Share**

Total net loss for the year ended December 31, 2010 amounted to €19.1 million, compared to the net loss for the year ended December 31, 2009 of €17.2 million, an increase of €1.9 million. The increase in the net loss includes an increase in non-cash charges of €1.2 million described within the 'Operating loss' and 'Finance income and costs' paragraphs above. The loss per share amounted to €1.13 for 2010 compared to €1.17 for 2009. The basic and diluted loss per share are the same because the company is loss-making in both periods.

### **Cash Flow and Cash Position**

Cash and cash equivalents amounted to €17.9 million at December 31, 2010, a decrease of €4.8 million or 21% compared to €22.6 million at December 31, 2009. The decrease in cash and cash equivalents is mainly the result of cash used in operating activities amounting to €17.7 million in 2010 (2009: €16.5 million), offset by net cash generated from financing activities of €13.4 million.

The cash used in operating activities represents our operational loss adjusted for non-cash items such as share-based payment expenses and changes in working capital.

The cash flow from financing activities amounted to €13.4 million reflecting the issue of new shares in October 2010, compared to €4.8 million in 2009, which principally represented the drawdown of the convertible loan.

### **Equity**

Shareholders' equity amounted to €13.5 million at December 31, 2010 compared to €18.4 million at December 31, 2009. A total number of 23,512,225 shares were issued and outstanding at December 31, 2010.

**Financial Report**  
Report of the Management  
Board

## Outlook

The company expects its existing cash resources, together with the net cash inflows that it expects to generate during 2011 from partnering activities and from the commercialization of Glybera® that would follow a successful MAA submission, to be sufficient to fund its operations for at least the next 12 months from the date of publication of these audited consolidated annual accounts. In reaching this conclusion, the Management of AMT has considered the uncertainty inherent in forecasting future net cash inflows, and believes that its expectations, as described above, are reasonable.

In the event that the Company succeeds in generating additional net cash inflows, it may incur expenditure at a faster rate in order to accelerate the development of its programs where there is a realistic and attractive business case for doing so. To this end it carefully monitors the level of its commitments. Further details regarding the Company's assessment of its outlook are described in Note 2.1 to the financial statements.

## Risk Factors

The Company is exposed to specific industry risks, as well as general business risks. Listed below are the risks perceived to be the most significant. The risks we face are not limited to this list.

### Risks Related to the Business

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 effective in humans. Pre-clinical and clinical trials are expensive, can take many years and have an uncertain outcome. A failure of one or more of our clinical trials could occur at any stage of testing.

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

Any delay in commencing or completing clinical trials for our products would delay commercialization of our products and severely harm our business and financial condition. It is also possible that none of our products will 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. The 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.

Additional clinical trials may be required if clinical trial results are negative or inconclusive, which will require us to incur additional costs and significant delays.

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

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

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

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

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.

**Financial Report**  
Report of the Management  
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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 in the range of current innovative, new 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.

### **Risks Related to Our Company**

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. 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.

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 again achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

We expect to need additional funding in the future, 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.

Our current cash and cash equivalents balances will not be sufficient to finance our long term research, development and commercialization programs. Therefore, additional funds will be required. 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. Our inability to obtain additional funds necessary to operate the business could 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.

### **Control Statement**

The Company has developed an internal risk management and control system that is tailored to the risk factors that are relevant to the Company, allowing for its small size. The controls frequently entail involvement of the highest level of management in decision-making. The internal risk management and control systems were discussed between the Supervisory Board, the Audit Committee and the Management Board. The Management Board believes that in respect of financial reporting risks: (i) in 2010 the risk management and control systems provide for a reasonable level of certainty that the financial reporting does not contain any material inaccuracies; and (ii) in 2010 the risk management and control systems have functioned properly.

### **Internal Risk Management and Control System**

AMT's Management Board is responsible for designing, implementing and operating the Company's internal risk management and control systems. The purpose of these systems is to manage in an effective and efficient manner the significant risks to which the Company is exposed. The Company's internal risk management and control systems are designed to provide reasonable assurance that strategic objectives can be met. Such systems can never provide absolute assurance regarding achievement of Company objectives, nor can they provide an absolute assurance that material errors, losses, fraud, and the violation of laws or regulations will not occur. A summary of the risks that could prevent AMT from realizing its objectives is included in the section 'Risk Factors' of this report.

Our internal risk management and control systems make use of various measures including:

Annual strategic evaluations of our business;

- Periodic operational review meetings of the Management Board with the Management Committee;
- Quarterly review of the financial position and prospects as part of the meetings of the Management Board with the Supervisory Board;
- A planning and control cycle consisting of annual, quarterly and monthly procedures, including subsequent follow-up on achievements of targets set;
- Advice of AMT's Disclosure Committee to our Chief Executive Officer and Chief Financial Officer with respect to the timely review, disclosure and evaluation of material issues and events;

## Financial Report

Report of the Management  
Board

- An effective system of internal controls and procedures is maintained;
- An Audit Committee that meets regularly with each of the Management Board and the external auditors; and
- Management letters and audit reports provided by our external auditor.

The Company maintains records and procedures designed to:

- Ensure the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and disposition of the assets of the Company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only by authorized employees in accordance with documented authorizations; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness for future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

Management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2010.

Based on its assessment and those criteria, Management concluded that the Company maintained effective internal control over financial reporting as of December 31, 2010.

### Changes in Internal Control over Financial Reporting

There has not been any change in the internal controls over financial reporting of the Company that occurred during the period covered by this report that has materially affected, or is reasonably likely to materially affect, such internal controls over financial reporting.

On this basis, the Company believes to be compliant with the best practice recommendations II.1.4 and II.1.5 of the Dutch Corporate Governance Code taking into account the most recent recommendations of the Monitoring Commission Corporate Governance as published on January 23, 2010. Further information on the application of the Dutch Corporate Governance Code is set out on pages 22 to 30 of these accounts.

## **Director's Statement**

The financial statements for 2010 for Amsterdam Molecular Therapeutics (AMT) Holding N.V. have been prepared in accordance with International Financial Reporting Standards as adopted by the European Union and, in our opinion, give a true and fair view of the Group's and the Company's financial position at December 31, 2010 and of the results of the Group's and the Company's operations and cash flows for the financial year 2010. In our opinion, the report of the Management Board gives a true and fair view of the Group's and the Company's financial position at December 31, 2010, the course of business in the financial year 2010 and of the most significant risks the Group and the Company are faced with.

Jörn Aldag  
Chief Executive Officer

Piers Morgan  
Chief Financial Officer





# Consolidated Balance Sheet

Amounts in € x 1,000 (after appropriation of result)

<b>Assets</b>			
	<b>Note</b>	<b>31.12.2010</b>	<b>31.12.2009</b>
<b>Non-current assets</b>			
Intangible assets	(5)	2,916	3,008
Property, plant and equipment	(6)	1,286	1,756
		<b>4,202</b>	<b>4,764</b>
<b>Current assets</b>			
Receivables from related parties	(7)	35	34
Social security and other taxes	(7)	409	414
Other receivables	(7)	198	469
Cash and cash equivalents	(8)	17,859	22,624
		<b>18,501</b>	<b>23,541</b>
<b>Total assets</b>		<b>22,703</b>	<b>28,305</b>

<b>Equity</b>			
Share capital		940	592
Share premium		99,136	88,074
Other reserves		1,788	831
Retained earnings	(9)	(88,205)	(69,087)
<b>Total group equity</b>		<b>13,659</b>	<b>18,410</b>

<b>Liabilities</b>			
<b>Non-current liabilities</b>			
Financial lease liabilities	(10)	221	259
Debt to related party	(11)	4,621	4,723
		<b>4,842</b>	<b>4,982</b>
<b>Current liabilities</b>			
Trade payables	(12)	1,556	1,182
Social security and other taxes	(12)	196	215
Other current liabilities	(12)	2,450	3,516
		<b>4,202</b>	<b>4,913</b>
<b>Total liabilities</b>		<b>9,044</b>	<b>9,895</b>
<b>Total equity and liabilities</b>		<b>22,703</b>	<b>28,305</b>

The selected Notes on pages 60 to 92 are an integral part of these consolidated financial statements.

# Consolidated Income Statement

Amounts in € x 1,000

	Note	31.12.2010	31.12.2009
Other income	(13)	1,448	355
<b>Total net income</b>		<b>1,448</b>	<b>355</b>
Research and development costs	(14, 15)	(16,404)	(13,241)
General and administrative costs	(14, 15)	(4,113)	(4,913)
<b>Total operating costs</b>		<b>(20,517)</b>	<b>(18,154)</b>
<b>Operating result</b>		<b>(19,069)</b>	<b>(17,799)</b>
Finance income	(16)	472	647
Finance costs	(16)	(521)	(23)
		<b>(49)</b>	<b>624</b>
<b>Result before corporate income taxes</b>		<b>(19,118)</b>	<b>(17,175)</b>
Corporate income taxes	(17)	–	–
<b>Result for the year</b>		<b>(19,118)</b>	<b>(17,175)</b>
<b>Attributable to:</b>			
<b>Ordinary shareholders of the Company</b>		<b>(19,118)</b>	<b>(17,175)</b>
<b>Earnings per share for result attributable to the equity holders of the Company during the period (expressed in Euro per share)</b>			
<b>Basic and diluted earnings per share</b>	(18)	<b>(1.13)</b>	<b>(1.17)</b>

The selected Notes on pages 60 to 92 are an integral part of these consolidated financial statements.

# Consolidated Statement of Comprehensive Income

Amounts in € x 1,000

	31.12.2010	31.12.2009
Result for the period	(19,118)	(17,175)
Other comprehensive income	–	–
<b>Total comprehensive result for the period</b>	<b>(19,118)</b>	<b>(17,175)</b>
<b>Attributable to:</b>		
<b>Equity holders of the Company</b>	<b>(19,118)</b>	<b>(17,175)</b>

The selected Notes on pages 60 to 92 are an integral part of these consolidated financial statements.

## Consolidated Statement of Changes in Equity

Amounts in € x 1,000

	Note	Share capital	Share premium reserve	Other reserves	Retained earnings	Total equity
<b>Balance at January 1, 2009</b>		<b>587</b>	<b>86,039</b>	<b>391</b>	<b>(51,912)</b>	<b>35,105</b>
Result for the year					(17,175)	(17,175)
Capital contributions	(9)	5	35			40
Share-based payment expenses	(9)			440		440
<b>Balance at December 31, 2009</b>		<b>592</b>	<b>86,074</b>	<b>831</b>	<b>(69,087)</b>	<b>18,410</b>
<b>Balance at January 1, 2010</b>		<b>592</b>	<b>86,074</b>	<b>831</b>	<b>(69,087)</b>	<b>18,410</b>
Result for the year					(19,118)	(19,118)
Capital contributions		348	13,062			13,410
Share-based payment expenses				957		957
<b>Balance at December 31, 2010</b>		<b>940</b>	<b>99,136</b>	<b>1,788</b>	<b>(88,205)</b>	<b>13,659</b>

The selected Notes on pages 60 to 92 are an integral part of these consolidated financial statements.

# Consolidated Cash Flow Statement

Amounts in € x 1,000

	Note	31.12.2010	31.12.2009
<b>Cash flow from operating activities</b>			
Result before corporate income tax adjustments for:		(19,118)	(17,175)
– Depreciation and amortisation	(6)	685	688
– Impairment of assets		472	–
– Derivative result		(220)	–
– Exchange result		127	–
– Share-based payment expenses	(9)	957	440
– Changes in working capital		(440)	165
– Interest (income)/expense	(16)	142	(624)
Cash used in operations		(17,395)	(16,506)
Interest paid	(16)	(256)	(23)
<b>Net cash generated from operating activities</b>		<b>(17,651)</b>	<b>(16,529)</b>
<b>Cash flow from investing activities</b>			
Purchases of property, plant and equipment	(6)	(387)	(106)
Purchases of intangible fixed assets	(5)	(208)	(511)
Interest received	(16)	71	857
<b>Net cash used in investing activities</b>		<b>(524)</b>	<b>240</b>
<b>Cash flow from financing activities</b>			
Capital contribution shareholders	(9)	13,410	40
Convertible loans drawn down, net of costs	(11)	–	4,723
<b>Net cash generated from financing activities</b>		<b>13,410</b>	<b>4,763</b>
<b>Net (decrease)/increase in cash, cash equivalents and other bank overdrafts</b>		<b>(4,765)</b>	<b>(11,526)</b>
Cash, cash equivalents and bank overdrafts at the beginning of the year	(8)	22,624	34,150
<b>Cash, cash equivalents at the end of the year</b>		<b>17,859</b>	<b>22,624</b>

The selected Notes on pages 60 to 92 are an integral part of these consolidated financial statements.

# Notes to the Consolidated Financial Statements

## 1. General Information

Amsterdam Molecular Therapeutics (AMT) Holding N.V. (“AMT” or “the Company”) is a biopharmaceutical Company with its statutory seat in Amsterdam that develops gene-based therapies. The Company’s gene therapy products offer long-term expression of a therapeutic gene thereby correcting the underlying genetic defect that causes the disease, whereas existing treatments only treat symptoms and subsequent medical complications.

The Company was founded in 1998 by scientists who were investigating lipoproteinlipase (LPL) deficiency at the Academic Medical Center (the “AMC”) of the University of Amsterdam, one of the largest academic hospitals in the world. The Company is located on the premises of the AMC and employs 83 highly educated individuals with scientific and industrial experience.

In July 2006, the Company raised €22 million of funds through an independent finance round from a group of four venture capital investors (“private equity financing”), primarily for the clinical development of our LPL deficiency gene therapy (the investors were Advent Venture Partners, Crédit Agricole Private Equity, Forbion Capital Partners and Gilde Healthcare Partners).

On June 20, 2007 the Company completed its Initial Public Offering (IPO) of shares on the Euronext Amsterdam stock exchange, generating gross proceeds of €55,674,000.

On October 6, 2010 the Company issued 8,435,294 new shares to existing and new shareholders at a premium of €1.70 per new share, by way of a private placement at the then market value of AMT Shares, generating gross proceeds of €14,340,000.

The Company’s major shareholders are:

- Advent Venture Partners
- Crédit Agricole Private Equity
- Forbion Capital Partners
- Gilde Healthcare Partners

The Company’s business is not subject to seasonal influences.

The financial statements were approved for issue by both the Supervisory Board and the Board of Management on March 4, 2011.

## 2. Summary of Significant Accounting Policies

The principal accounting policies applied in the preparation of these consolidated financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

### 2.1 Basis of Preparation

The consolidated financial statements of AMT and its subsidiaries (together “the Group”) have been prepared in accordance with International Financial Reporting Standards, as endorsed by the European Union, (“IFRS”).

The consolidated financial statements have been prepared under the historical cost convention, except for financial instruments and share-based payment obligations which have been based on fair value. Furthermore, the consolidated financial statements are presented in Euros and all values are rounded to the nearest thousand except where otherwise indicated.

Amsterdam Molecular Therapeutics (AMT) Holding N.V. is 100% owner and controller of two subsidiaries, Amsterdam Molecular Therapeutics (AMT) B.V. and Amsterdam Molecular Therapeutics (AMT) IP B.V., and also controls the Stichting Participatie AMT, a trust foundation which is used to effect the issue of Depositary Receipts. These three entities, together with Amsterdam Molecular Therapeutics (AMT) Holding N.V., are consolidated within the AMT consolidated accounts.

The preparation of financial statements in conformity with IFRS requires the use of certain critical accounting estimates. It also requires management to exercise its judgement in the process of applying the Group’s accounting policies. The areas involving a higher degree of judgement or complexity or areas where assumptions and estimates are significant to the consolidated financial statements are disclosed in Note 4.

New standards, amendments and interpretations to existing IFRS standards became effective in 2010, the most important of which are:

- IFRS 3 (revised) ‘Business Combinations’. The revised standard continues to apply the acquisition method to business combinations but with some significant changes compared with IFRS 3. The new standard applies prospectively for new business combinations as of 2010. The group did not enter into any business combinations in 2010.
- IAS 27, ‘Consolidated and Separate Financial Statements’. The effects of all transactions with non-controlling interests are recorded in equity if there is no change in control and these transactions will no longer result in goodwill or gains and losses. When control is lost, any remaining interest in the entity is re-measured to fair value, and a gain or loss is recognized in profit or loss. The change in accounting policy is applied prospectively. AMT currently has no non-controlling interests in its subsidiaries.

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### Notes to the Consolidated Financial Statements

- Other new standards, amendments and interpretations did not have an impact on the accounting policies of AMT.

The International Accounting Standards Board (IASB) has issued a number of new standards, amendments and interpretations which will become effective for AMT as of January 1, 2011 or later. These have not been applied in preparing these 2010 Consolidated Financial Statements. The most relevant changes for AMT relate to IFRS 9, 'Financial instruments'; 'Classification of rights issues' (amendment to IAS 32), and IFRIC 19, 'Extinguishing financial liabilities with equity instruments'. These new standards, amendments and interpretations are expected to have no material impact on the valuation and classification of assets and liabilities of the Group, nor on its income statement or cash flows.

The IASB has also issued Exposure Drafts in which significant changes on accounting and disclosures are proposed on topics like lease accounting and revenue recognition. If the current proposals lead to new or amended standards, the changes could have a substantial impact on our financial statements in the coming years. The effective date of the revised standards is still under discussion.

#### Going concern

The company expects its existing cash resources, together with the net cash inflows that it expects to generate during 2011 from partnering activities and from the commercialization of Glybera® that would follow a successful MAA submission, to be sufficient to fund its operations for at least the next 12 months. As at the date of these accounts, the existing cash resources of the Company are not sufficient to fully cover the projected expenditure over the coming 12 months. Historically the Company has not generated sufficient cash from commercial activities to meet its current working capital requirements and has been since its incorporation largely dependent on financing arrangements with third parties.

Taking into account the potential sources of revenue available to the Company, the Company expects to secure sufficient additional net cash inflows, and accordingly these accounts have been prepared on a going concern basis. In the event that additional cash inflows are not secured, the Company expects that it will need to take appropriate action to reduce its costs, and this may result in the Company no longer being in a position to progress some or all of its programs. Reducing the Company's spend in this way would provide a longer opportunity to seek an alternative solution, but would not provide any guarantee that a satisfactory long-term solution would be achieved. In case the Company is not able to attract sufficient additional cash it may not be able to continue as a going concern. Such an event could have a material impact on the carrying value of its assets.

Overall, based on the outcome of this assessment, these financial statements have been prepared on a going concern basis. Notwithstanding their belief and confidence that the Company will be able to continue as a going concern, Management emphasizes that the actual cash flows for various reasons may ultimately (significantly) deviate from their projections. Therefore, in a negative scenario (actual cash inflows less than projected and/or actual cash outflows higher than projected) the going concern of the Company could be at risk.



## **2.2 Consolidation**

Subsidiaries comprise all entities over which the Group has the power to control the financial and operating policies. Subsidiaries and special purpose vehicles are fully consolidated from the date on which control is transferred to the Group. Subsidiaries are de-consolidated from the date that control ceases.

Intercompany transactions and balances within the Group are eliminated. The accounting policies as applied by subsidiaries are consistent with the accounting policies applied by the Company.

## **2.3 Segment Reporting**

Operating segments are identified on the basis of whether the allocation of resources and/or the assessment of performance of a particular component of the Group's activities are regularly reviewed by the Group's chief operating decision maker as a separate operating segment. By these criteria, the activities of the Group are considered to be one segment, and the segmental analysis is the same as the analysis for the Group as a whole.

## **2.4 Foreign Currency Translation**

### **(a) Functional and Presentation Currency**

Items included in the financial statements of each of the Group's entities are measured using the currency of the primary economic environment in which the entity operates ("the functional currency"). The consolidated financial statements are presented in Euros, which is the Company's functional and presentation currency.

### **(b) Transactions and Balances**

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognised in the income statement.

## **2.5 Intangible Assets**

### **(a) Licenses**

Acquired patents have a definite useful life and are carried at cost less accumulated amortisation and impairment losses. Amortisation is calculated using the straight-line method to allocate the cost of licenses over their estimated useful lives (generally 20 years unless a license expires prior to that date). Amortisation begins when an asset is available for use.

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#### (b) Research and Development

Research expenditures are recognised as expenses as incurred. Costs incurred on development projects are recognised as intangible assets as of the date that it can be established that it is probable that future economic benefits that are attributable to the asset will flow to the Company considering its commercial and technological feasibility, generally when filed for regulatory approval for commercial production, and when costs can be measured reliably. Given the current stage of the development of our products no development expenditures have yet been capitalized. Registration costs for patents are part of the expenditures for the research and development project. Therefore, registration costs for patents are expensed as incurred as long as the research and development project concerned does not yet meet the criteria for capitalization.

#### 2.6 Property, Plant and Equipment

Property, plant and equipment comprise mainly laboratory equipment, leasehold improvements, furniture and computer hardware and software. All property, plant and equipment are stated at historical cost less depreciation. Historical cost includes expenditures that are directly attributable to the acquisition of the items.

Subsequent costs are included in the asset's carrying amount or recognised as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. All other repairs and maintenance charges are expensed in the financial period in which these are incurred.

Depreciation is calculated using the straight-line method to allocate the cost of the assets to their residual values over their estimated useful lives. Property, plant and equipment are depreciated as follows:

- Leasehold improvements 5–15 years
- Laboratory equipment 5–10 years
- Computer hardware/software 3 years

The assets' residual values and useful lives are reviewed, and adjusted if appropriate, at each balance sheet date. An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is greater than its estimated recoverable amount (also refer to 2.7).

Gains and losses on disposals are determined by comparing proceeds with the carrying amount and are recognized in the income statement.

#### Financial Leases

Leases of property, plant and equipment where the Group bears substantially all the risks and rewards of ownership are classified as financial leases. Financial leases are capitalized at the commencement of the lease at the lower of the fair value of the leased property and the present value of the minimum lease payments.

Each lease payment is allocated between the liability and finance charges so as to achieve a constant rate on the finance balance outstanding. The corresponding rental obligations, net of finance charges, are included in “finance lease liabilities”. The interest element of the finance cost is charged to the income statement over the lease period so as to produce a constant periodic rate of interest on the remaining balance of the liability for each period. The property, plant and equipment acquired under finance leases are depreciated over the shorter of the useful life of the asset or the lease term.

## **2.7 Impairment of Non-Financial Assets**

Assets that are not subject to amortisation (whether or not they are ready for use) are tested annually for impairment. Assets that are subject to amortisation are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. An impairment loss is recognised for the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value less costs to sell and value in use. For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units). Non-financial assets that have been previously impaired are reviewed for possible reversal of the impairment at each subsequent reporting date.

## **2.8 Trade Receivables**

Trade receivables are amounts due from customers for merchandise sold or services performed in the ordinary course of business. If collection is expected in one year or less (or in the normal operating cycle of the business if longer), they are classified as current assets. If not, they are presented as non-current assets.

Trade receivables are recognised initially at fair value and subsequently measured at amortised cost using the effective interest method, less provision for impairment.

## **2.9 Cash and Cash Equivalents**

Cash and cash equivalents include cash-in-hand, current accounts, deposits held at call with banks, other short-term highly liquid investments with original maturities of three months or less, and bank overdrafts. Bank overdrafts are shown separately within current liabilities on the balance sheet.

## **2.10 Equity and Borrowings**

### **Compound Instruments**

A financial instrument or its component parts are classified on initial recognition as a financial liability or a financial asset or an equity instrument in accordance with the substance of the contractual arrangement and the definitions of a financial liability

## Financial Statements

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### Financial Statements

or a financial asset and an equity instrument. An equity instrument is defined as any contract that evidences a residual interest in the assets of an entity after deducting all of its liabilities.

#### Convertible Loan

Where the Company issues convertible loans that do not have the unconditional right to avoid delivering cash or a variable number of shares to settle obligations towards loan note holders, the Company accounts for such loan notes as containing an element that qualifies as a financial liability. Convertible loans are split into a debt component and a separate conversion option component. The debt component is recognized initially at fair value, being the expected discounted value of the cash outflow required to settle the obligation using a market interest rate for an equivalent liability. The conversion option is the residual amount after deducting from the fair value of the loan as a whole (i.e. the issuance proceeds) the amount separately determined for the debt component. The debt component is subsequently carried at amortised cost using the effective interest rate method. When estimates regarding the amount or timing of payments required to settle the obligation change, the carrying amount of the financial liability is adjusted to reflect actual and revised estimated cash flows. The carrying amount is recalculated by computing the present value of estimated future cash flows at the financial instrument's original effective interest rate. Such adjustments are recognized as income or expense in the profit and loss account. Any costs of the loan are deducted from the carrying amount and are amortized over the term of the convertible loan under the effective interest rate method.

The conversion option is classified as a liability if it may be settled by either party other than by the exchange of a fixed amount of cash for a fixed number of the entity's own equity instruments. In that case the conversion option is carried at fair value with changes in fair value recorded in the income statement. If the conversion option qualifies as an equity instrument it is recognized in equity on issue date and not remeasured.

#### Ordinary Shares

Ordinary shares are classified as equity. Incremental costs directly attributable to the issue of new shares or options are shown in equity as a deduction from the proceeds, net of tax.

### 2.11 Trade Payables

Trade payables are obligations to pay for goods or services that have been acquired in the ordinary course of business from suppliers. Accounts payable are classified as current liabilities if payment is due within one year or less (or in the normal operating cycle of the business if longer). If not, they are presented as non-current liabilities.

Trade payables are recognized initially at fair value and subsequently measured at amortized cost using the effective interest method.

## **2.12 Deferred Corporate Income Taxes**

Deferred corporate income tax is recognized, using the liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the consolidated financial statements. Deferred corporate income tax is determined using tax rates (and laws) that have been enacted or substantially enacted by the balance sheet date and are expected to apply when the related deferred corporate income tax asset is realised or the deferred corporate income tax liability is settled. Deferred corporate income tax assets are recognized to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilised.

## **2.13 Employee Benefits**

### **(a) Pension Obligations**

The Group operates a defined contribution pension plan for all employees funded through payments to an insurance company. The Group has no legal or constructive obligation to pay further contributions if the plan does not hold sufficient assets to pay all employees the benefits relating to employee service in the current and prior periods. The contributions are recognised as employee benefit expense when they are due. Prepaid contributions are recognised as an asset to the extent that a cash refund or a reduction in the future payments is available.

### **(b) Share-based Compensation**

The Company operates two share-based payment plans. The first plan is a share incentive plan under which shares have been granted in 2006, 2007, 2008, 2009 and 2010. The second plan is an equity settled share option plan under which options have been granted in 2010.

The cost of employee cash-settled share-based compensation plans is measured by reference to the fair value of the options and the shares at the date at which the options are granted using a Binomial option valuation model. The cost of employee cash-settled share-based compensation plans is determined by the difference between the share price for an AMT share as per the date of grant and the discounted purchase price to be paid by the participants.

The fair value of the employee services received in exchange for the grant of the options is recognised as an expense. The total amount to be expensed over the vesting period, if any, is determined by reference to the fair value of the options granted. For the equity-settled option plan, the fair value is determined at the grant date, whereas for the cash-settled share plan, the liability is re-measured at each balance sheet date. For share-based payments that do not vest until the employees have completed a specified period of service, AMT recognises the services received as the employees render service during that period. The Company treats each instalment of a graded vesting award as a separate share option grant.

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At each balance sheet date, the Company revises its estimates of the number of options that are expected to become exercisable. It recognises the impact of the revision of original estimates, if any, in the income statement and a corresponding adjustment to equity. Until the liability resulting from the cash-settled plan is settled, the Company re-measures the fair value of the liability at each reporting date and at the date of settlement, with any change in fair value recognised in the income statement.

The equity settled share option plan commenced in 2010. At the balance sheet date 1,354,150 options are outstanding. The cost recognized in the comprehensive statement of income and expense for the equity settled share option plan is the amortization of the fair value of the outstanding options. The fair value is calculated at the grant date. The calculation method used is Black-Scholes. The amortization period is equal to the period between the grant date and vesting date. The share options' vesting periods are as follows: 50% vests after 3 years, 25% after 4 years, 25% after 5 years.

#### (c) Bonus Plans

The Group recognises a liability and an expense for bonus plans if contractually obliged or if there is a past practice that has created a constructive obligation.

## 2.14 Provisions

Provisions are recognized when the Group has a present legal or constructive obligation as a result of past events; it is probable that an outflow of resources will be required to settle the obligation; and the amount can be reliably estimated.

## 2.15 Revenues and Other Income

The Group's revenues comprise development services provided to third parties. Sales of services are recognised in the accounting period in which the services are rendered.

The Group's other income comprises certain subsidies which support the Group's research efforts in defined research and development projects. These subsidies generally provide for reimbursement of approved costs incurred as defined in various grants. Subsidies are recognised at their fair value when there is a reasonable assurance that the subsidy will be received and the Group will comply with all attached conditions.

## 2.16 Operating Leases

Leases in which a significant portion of the risks and rewards of ownership are retained by the lessor are classified as operating leases. Payments made under operating leases (net of any incentives received from the lessor) are charged to the income statement on a straight-line basis over the period of the lease.

## **2.17 Dividend Distribution**

Dividend distribution to the Company's shareholders is recognised as a liability in the Group's financial statements in the period in which the dividends are approved by the Company's shareholders.

## **2.18 Grants and Investment Credits**

Grants or Investment Credits may be repayable if the Group successfully commercialises a relevant program (which was funded in whole or in part by the Grant or Investment Credit) within a particular timescale. Once a program is commercialised, the Group will negotiate with the funder the basis for any such repayment and will determine the appropriate accounting treatment for the repayment at that time. Prior to successful commercialisation the Group does not make any provision for repayment.

# **3. Financial Risk Management**

## **3.1 Financial Risk Factors**

The Group's activities expose it to a variety of financial risks: market risk (including currency risk, fair value interest rate risk, cash flow interest rate risk and price risk), credit risk and liquidity risk. The Group's overall risk management program focuses on the unpredictability of financial markets and seeks to minimize potential adverse effects on the Group's financial performance.

Risk management is carried out by the finance department. The finance department identifies and evaluates financial risks and hedges these risks if deemed appropriate.

### **(a) Market Risk**

Foreign exchange risk arises from future commercial transactions and recognized assets and liabilities in foreign currencies. In the years presented, the Group had no significant outstanding receivables or payables in currencies other than Euros. In the absence of significant foreign exchange exposure, management has not set up a policy to manage the foreign exchange risk against the functional currency. The Group is not exposed to equity securities price risk since it does not hold any such investments, nor is the Group exposed to commodity price risk.

At December 31, 2010, there would not have been a significant effect on the Company's loss due to strengthening or weakening of the functional currency against any foreign currency.

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### (b) Credit Risk

The Company has no large receivable balances with external parties. At December 31, 2010 and December 31, 2009, the majority of the Company's cash and cash equivalents were placed at the following banks.

Amounts in € x 1,000

Bank	31.12.2010		31.12.2009	
	Amount (in € 1,000)	Credit rating (Moody's)	Amount (in € 1,000)	Credit rating (Moody's)
Rabo Bank	7,235	AAA	7,028	AAA
Van Lanschot	341	Aa3	–	–
Deutsche Bank	10,283	Aa3	15,010	Aa3

### (c) Liquidity Risk

Management considers the Company's liquidity reserve per December 31, 2010 sufficient to carry out the business plans going forward, at least until March 31, 2012. Prudent liquidity risk management implies maintaining sufficient cash, and planning to raise cash if and when needed, either through issue of shares or through credit facilities. Management monitors rolling forecasts of the Group's liquidity reserve on the basis of expected cash flow.

The table below breaks down the Group's financial liabilities into relevant maturity groups based on the remaining period at the balance sheet date to the contractual maturity date. The amounts disclosed in the table are the contractual undiscounted cash flows. Balances due within 12 months equal their carrying balances as the impact of discounting is not significant. On 23 December 2009 the Company issued € 5,000,000 in 5 year convertible loan notes to one of its shareholders, Forbion.

Amounts in € x 1,000

	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years
<b>31.12.2010</b>				
Trade and other payables	4,452	250	5,500	–
<b>31.12.2009</b>				
Trade and other payables	5,163	250	5,750	–

### (d) Cash Flow and Fair Value Interest Rate Risk

The Group has neither significant long-term interest-bearing assets nor significant long-term interest bearing liabilities other than the € 5,000,000 convertible loan described in Note 2.10.



### 3.2 Capital Risk Management

The Group's objectives when managing capital are to safeguard the Group's ability as a going concern in order to provide returns for shareholders and benefits for other stakeholders and to maintain an optimal structure to reduce the cost of capital.

In order to maintain or adjust the capital structure, the Group may return capital to shareholders, issue new shares or sell assets to reduce debt.

## 4. Critical Accounting Estimates and Judgements

Estimates and judgements are continually evaluated and are based on historical experience and other factors, including expectations of future events that are believed to be reasonable under the circumstances.

The Group makes estimates and assumptions concerning the future. The resulting accounting estimates will, by definition, seldom equal the related actual results. The estimates and assumptions that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year as well as critical judgements in applying the Group's accounting policies, are discussed below.

### (a) Corporate Income Taxes

The Group, which has a history of recent tax losses, recognises deferred tax assets arising from unused tax losses or tax credits only to the extent that the relevant fiscal unity has sufficient taxable temporary differences or there is convincing other evidence that sufficient taxable profit will be available against which the unused tax losses or unused tax credits can be utilised by the fiscal unity. Management's judgement is that sufficient convincing other evidence is not available and a deferred tax asset is therefore not recognised.

### (b) Share-Based Payments

During 2009 all remaining granted share options that had been outstanding under the company's original cash settled share option schemes lapsed. No further revaluation was required. The option liability as at December 31, 2008 of € 17,000 was released during the year ended December 31, 2009.

In 2010 the Company introduced a new equity settled share option scheme. The equity settled share option plan commenced in 2010. At balance sheet date 1,354,150 options are outstanding. The cost recognized in the income statement and expense for the equity settled share option plan is the amortization of the fair value of the outstanding options. The fair value is calculated at the grant date. The calculation method used is Black-Scholes. The amortization period is equal to the period between the grant date and vesting date. The share options vesting periods are as follows: 50% vests after 3 years, 25% after 4 years, 25% after 5 years.

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#### (c) Research and Development Expenditures

The project stage forms the basis for the decision whether costs incurred for the Company's research and development projects can be capitalized or not. In general, AMT's vision is that clinical development expenditures are not capitalized until marketing approval (i.e. approval to commercially use the product; for example the final FDA approval in the US or market authorization with EMA in the EU) is obtained, as this is essentially the first point in time where it becomes probable that future revenues can be generated (and the project becomes commercially successful).

#### (d) Impairment of Assets

Assets that are subject to amortisation are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. In the year ended December 31, 2010, management recognized an impairment in the value of fixed assets amounting to €172,000 in respect of capitalized leasehold improvements which were no longer required for activities of the group. In addition an impairment charge of a further €300,000 was made in respect of the termination of a research and license agreement under which AMT 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.

Assets that are not subject to amortization are tested annually for impairment. For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units). Currently, all material assets are used in the development of certain gene therapy products, mainly in the field of LPL deficiency. Therefore, the activities of the Company are regularly reviewed by the chief operating decision maker as a single component and one cash-generating unit. No products are sold on the market yet and future profits and cash flows are fully dependent on whether approval for market introduction is obtained.

Based on management's expectations of revenues and gross margin as from market introduction, when and if obtained, no impairment charge is deemed necessary. These expectations are mainly based on management's estimate of size of the market size for the product that is being developed and the gross margin that will be realized.

#### (e) Compound Financial Instruments

A financial instrument or its component parts are classified on initial recognition as a financial liability, a financial asset or an equity instrument in accordance with the substance of the contractual arrangement and the definitions of a financial liability, a financial asset and an equity instrument. As described under paragraph 2.10 we have analysed the convertible loan issued in 2009 and concluded that both the loan and the convertible elements qualified as financial liabilities.

## 5. Intangible Assets

Amounts in € x 1,000

	Licences
<b>At January 1, 2009</b>	
Cost	2,497
Accumulated amortisation and impairment	–
<b>Net book amount</b>	<b>2,497</b>
<b>Year ended December 31, 2009</b>	
Opening net book amount	2,497
Additions	511
Amortisation charge	–
<b>Closing net book amount</b>	<b>3,008</b>
<b>At December 31, 2009</b>	
Cost	3,008
Accumulated amortisation and impairment	–
<b>Net book amount</b>	<b>3,008</b>
<b>Year ended December 31, 2010</b>	
Opening net book amount	3,008
Additions	208
Amortisation and impairment charge	(300)
<b>Closing net book amount</b>	<b>2,916</b>
<b>At December 31, 2010</b>	
Cost	3,216
Accumulated amortisation and impairment	(300)
<b>Net book amount</b>	<b>2,916</b>

AMT obtained a sub-license from Xenon (approved by the licensor The University of British Columbia) in June 2001 which was initially capitalized for an amount of €140,000. Xenon granted AMT the exclusive worldwide rights to use the Xenon Licensed Technology and to use, manufacture, distribute and sell Licensed Products. In addition to the license fee, milestone payments are recognized under the contract. Dependent upon the progress and success of the research and development activities and sales by the Company future milestones are capitalized when payment is probable. In 2006, a milestone of €70,000 was paid and capitalized. Amortization will commence when the related product which is currently being developed by the Company, is available for use, in this case by market introduction.

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In December 2006 the Company acquired a sub-license from Targeted Genetics, Inc. (approved by the licensor The University of Pennsylvania) related to “AAV1 Vector” technology for an amount of € 1,330,000. In 2008, a milestone payment of € 357,000 was paid and added to intangible fixed assets. Amortization will commence when the related product which is currently being developed by the Company, is available for use, in this case by market introduction.

In 2008, the Company paid and capitalized licensing fees totalling € 600,000 related to a license from the “La Sapienza” university of Rome for technology for treatment for Duchenne Muscular Dystrophy and a licence from the “San Raffaele” university of Milano for technology to be used in the treatment of Factor IX Hemophilia.

In 2009 the Company accrued for a licensing milestone of \$ 750,000 to Targeted Genetics, Inc. which became payable on the submission of the Marketing Authorisation Application of Glybera® to EMA.

In 2010 the Company acquired a license from National Institute of Health in the amount of € 208,000 for the production of Adeno-Associated Virus. The Company also terminated a research and license agreement under which AMT had made an initial payment of € 300,000 in respect of the licence from “San Raffaele” university of Milano. This payment had been capitalized as an intangible asset, and accordingly this amount has been written off, as described in the note 4(d) above.

In the years presented in these financial statements, no amortisation on the other licenses is recorded since the related products for which the licenses have been granted are not yet available for use. Management estimates at the end of each annual reporting period the recoverable amount of these licenses, irrespective of whether there is any indication that the licenses may be impaired.

Management determined that based on its expectations of revenues and gross margin following market launch, no other impairment charge is necessary.

## 6. Property, Plant and Equipment

Amounts in € x 1,000

	Leasehold improvement	Laboratory equipment	Hardware/ software	Total
<b>At January 1, 2009</b>				
Cost	888	2,443	414	3,745
Accumulated amortisation and impairment	(191)	(1,003)	(213)	(1,407)
<b>Net book amount</b>	<b>697</b>	<b>1,440</b>	<b>201</b>	<b>2,338</b>
<b>Year ended December 31, 2009</b>				
Opening net book amount	697	1,440	201	2,338
Additions	5	56	45	106
Depreciation charge	(134)	(434)	(120)	(688)
<b>Closing net book amount</b>	<b>568</b>	<b>1,062</b>	<b>126</b>	<b>1,756</b>
<b>At December 31, 2009</b>				
Cost	893	2,499	459	3,851
Accumulated amortisation and impairment	(325)	(1,437)	(333)	(2,095)
<b>Net book amount</b>	<b>568</b>	<b>1,062</b>	<b>126</b>	<b>1,756</b>
<b>Year ended December 31, 2010</b>				
Opening net book amount	568	1,062	126	1,756
Additions	–	342	45	387
Depreciation charge	(60)	(527)	(98)	(685)
Impairment	(172)	–	–	(172)
<b>Closing net book amount</b>	<b>336</b>	<b>877</b>	<b>73</b>	<b>1,286</b>
<b>At December 31, 2010</b>				
Cost	721	2,841	504	4,066
Accumulated amortisation and impairment	(385)	(1,964)	(431)	(2,780)
<b>Net book amount</b>	<b>336</b>	<b>877</b>	<b>73</b>	<b>1,286</b>

Leasehold improvements include a net book value at December 31, 2010 of € 230,000 (2009: € 269,000) where the Group is lessee under a finance lease. Laboratory equipment includes a net book amount at December 31, 2010 of nil (2009: € 63,225) where the Group is lessee under a finance lease. The company impaired leasehold improvements which were of no longer use to the company for her current activities. Also refer to Note 10 for a description of the financial lease contracts.

The assets' residual values are reviewed, and adjusted if appropriate, at each balance sheet date. An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is greater than its estimated recoverable amount (also refer to 2.7). Following a review of Leasehold improvements, the estimated life of Leasehold improvements has been amended to 5–15 years (previously 10–15 years). This amendment reflects past practice, and has no impact on either the depreciation charge nor the financial position of the Company for the financial years ended December 31, 2010 and 2009 where the amount is nil.

## 7. Trade and Other Receivables

Amounts in € x 1,000

	31.12.2010	31.12.2009
Receivables from related parties (Note 23)	35	34
VAT to be received	221	204
Tax on wages to be received	175	197
Social Security to be received	13	13
<b>Total taxes and social securities</b>	<b>409</b>	<b>414</b>
Interest to be received	198	126
Prepaid expenses	–	334
Other receivables	–	9
<b>Other receivables and prepayments</b>	<b>198</b>	<b>469</b>

The carrying values of trade and other receivables are assumed to approximate their fair values.

## 8. Cash and Cash Equivalents

Amounts in € x 1,000

	31.12.2010	31.12.2009
Cash at bank and in hand	9,480	8,146
Short-term bank deposits	8,379	14,478
	<b>17,859</b>	<b>22,624</b>

The effective interest rate on short-term bank deposits was 1,5% in the year ended December 31, 2010 (2,3% in the year ended December 31, 2009); these deposits have an average maturity of 1 day.

## 9. Shareholders' Equity

Amounts in € x 1,000

	Number of shares	Amount of capital
<b>Share capital (ordinary shares)</b>		
At January 1, 2009	14,676,545	587
New shares issued	137,183	5
<b>At December 31, 2009</b>	<b>14,813,728</b>	<b>592</b>
New shares issued	8,698,497	348
<b>At December 31, 2010</b>	<b>23,512,225</b>	<b>940</b>

Following the Extraordinary General Meeting of Shareholders of AMT on September 20, 2010 the Company's authorised share capital was increased from € 1,000,000 to €1.3 million or 32,500,000 ordinary shares. At December 31, 2010 the issued share capital amounted to € 940,489, or 23,512,225 shares. Accordingly the authorised but unissued share capital amounted to € 359,511 or 8,987,775 ordinary shares.

On December 31, 2010 a total of 23,512,225 shares were issued and paid up in full at a nominal value of €0.04 per share (2009: €0.04 per share). Of these 8,698,497 were issued during the 12 months ended December 31, 2010. The total gross payment with respect to the issued ordinary shares amounted to €14,410,663.

On October 6, 2010 the Company issued €8,435,294 new ordinary shares to existing and new shareholders at a price of € 1.70 per share raising a total of € 14,340,000 before expenses. The company incurred cost in respect of this issue amounts to €1,000,000.

Additional shares were issued pursuant to Share incentive plans as described below.

In 2010 no new shares were issued upon exercise of stock options.

On September 30, 2010 263,203 new shares were issued in respect of the Share Incentive Plan to the Stichting which then issued corresponding number of depository receipts to certain Board members and employees.

On December 31, 2010 3,816 shares were held as treasury shares; these shares arose in respect of the Share Incentive Plan (as described in note 2.13 and this note 9) by Stichting Participatie AMT ("Stichting"), representing the repurchase of depository receipts from employees leaving the Company, and the consequent return of the beneficial rights in the underlying shares from the leaving employee to the Stichting.

At December 31, 2009 no shares were held as treasury shares.

## Share Premium

The total addition to share premium in the year ended December 31, 2010 amounts to € 13,062,000 net of cost (year ended December 31, 2009: € 35,000), reference is made to the movement schedule below:

Amounts in € x 1,000

	31.12.2010	31.12.2009
<b>Balance beginning of the period</b>	<b>86,074</b>	<b>86,039</b>
New shares issued	13,062	35
<b>Balance end of the period</b>	<b>99,136</b>	<b>86,074</b>

## Other Reserves

The costs of equity-settled share-based payments to employees are recognised in the income statement, together with a corresponding increase in equity during the vesting period, taking into account (deferral of) corporate income taxes. The accumulated expense of the share incentive plan recognised in the income statement is shown separately in the equity category “other reserves” in the “consolidated statement of changes in equity”. In the years presented in these financial statements, the Company did not have any legal or other types of restricted reserves.

## Share Options

### 2001 Stock Option Plan

In 2001, the Company set up a stock option plan (the 2001 Plan) under which no options were outstanding as of December 31, 2010 nor December 31, 2009, all remaining option. These options had been offered to personnel, consultants and management. Options remained valid for a period of 4 or 5 years after the grant date.

The stock option incentive plan from 2001 qualified as a cash-settled plan. Movements in the number of outstanding share options, all of which were granted in 2004, were as follows:

2004 grant	01.01. – 31.12.2010		01.01. – 31.12.2009	
	Number	Exercise price	Number	Exercise price
Number of options outstanding 1 January	–	–	52,095	2.63–3.29
Number of options lapsed	–	–	(52,095)	2.63–3.29
<b>Number of options outstanding 31 December</b>	<b>–</b>	<b>–</b>	<b>–</b>	<b>–</b>



## 2010 Stock Option Plan

At the Annual General Meeting of Shareholders on April 28, 2010 shareholders approved the creation of a new share-based payment plan (the 2010 Plan). Under the 2010 Plan share options are granted with an exercise price equal to the share price on the date of grant and vest over a period of 3–5 years subject to the following conditions:

- (i) 50% vest on the third anniversary of the date of grant, subject to a 50% increase in the price of AMT shares over the period from the date of grant. If the options fail to vest under this condition they are carried forward and retested under (ii) below;
- (ii) a further 25% vest on the fourth anniversary of the date of grant, subject to a 75% increase in the price of AMT shares over the period from the date of grant. Any options that have not vested under (i) or (ii) are carried forward and retested under (iii) below; and
- (iii) the final 25% vest on the fifth anniversary of the date of grant, subject to a 100% increase in the price of AMT shares over the period from the date of grant. Any options that have not vested on or before the fifth anniversary of grant lapse.

Any options that vest must be exercised by the tenth anniversary of the date of grant. The 2010 Plan qualifies as an equity-settled plan.

In 2010 1,387,000 options were granted to management and certain other employees under the 2010 Plan.

The 2010 Plan qualifies as an equity-settled plan. Movements in the number of outstanding share options, all of which were granted in 2010, were as follows:

2010 grant	31.12.2010		31.12.2009	
	Number	Exercise price	Number	Exercise price
Number of options outstanding 1 January	–	–	–	–
Number of options granted	1,387,000	2,92	–	–
Number of options lapsed	(32,850)	2,97	–	–
<b>Number of options outstanding 31 December</b>	<b>1,354,150</b>	<b>2,92</b>	<b>–</b>	<b>–</b>

The exercise price is a weighted average.

The weighted average fair-value for 2010 is €1.27.

A stochastic valuation model (a.k.a. Monte Carlo model) has been used to value these awards.

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The valuation model involves six key variables, as detailed on the next page:

Share Price: the closing share price on the grant dates, being €2.97 and €1.95.

Exercise Price: equal to the closing share price on the grant dates

Expected Term: is the period from grant until the expected exercise date. A fixed expected term of six years for the three year tranche, six and a half years for the four year tranche and seven years for the five year tranche, being part way between the vesting date and lapse date for each tranche.

Expected Volatility: AMT used a proxy volatility of 50%, a figure which was fixed based on volatility analysis of companies in the same sector and of a similar size.

Expected Dividend Yield: the Company currently does not pay dividends.

Risk-free Rate: based on Dutch Government bonds with a term commensurate with the expected term of each option tranche. Also considered is the risk-free rate over the performance period for each option tranche.

#### Share Incentive Plan

In 2006, the Company set up a new share incentive plan which qualifies as an equity-settled plan. Eligible employees are offered the purchase of Depositary Receipts of common shares of the Company. Under the plan, the Company offers Depositary Receipts to the employees against payment of a discounted price of 10% of the estimated fair market value for Dutch tax purposes at the date of award. The Depositary Receipts immediately entitle the holder to the full beneficial interest in the underlying shares, but do not entitle the holder to the voting rights. On this basis, the entire charge arising from the offering of Depositary Receipts to grantees is recognised on the date of grant.

In 2008, 14,103 Depositary Receipts were granted to management and certain other employees under the share incentive plan. A share-based payment expense amounting to €72,000 has been recognized for the difference between the value of an AMT Depositary Receipt, which is estimated based on the difference between the share price for an AMT share as per the date of the grant and the discounted purchase price to be paid by the participants. In 2008, 2,509 Depositary Receipts were forfeited by employees that left AMT.

In 2009, 137,183 Depositary Receipts have been granted to management and certain other employees under the share incentive plan. Under the terms of the Stock Option Plan, 137,183 new ordinary shares in the Company were issued to the Employee Share Trust (Stichting) against the 137,183 Depositary Receipts that were issued to staff. The depositary receipts may be exchanged for ordinary shares in the Company three years after the date of grant. If an employee leaves the Group voluntarily within three years from the date of grant, the Company has the right to repurchase the depositary receipts from the employee at the lower of the open market value of the shares or their nominal value (€ 0.04 per share).

In 2010, 263,203 Depositary receipts have been granted to management and certain employees (2009: 137,138). A share-based payment expense amounting to €635,790 has been recognized for the difference between the value of an AMT Depositary Receipt, which is estimated based on the difference between the share price for an AMT share as per the date of the grant and the discounted purchase price to be paid by the participants, as required by IFRS 2. 3,149 Depositary Receipts were forfeited by employees that left AMT (2009: 667). In 2010 41,452 depositary receipts were converted to ordinary shares (2009 nil). The fair value of the 263,203 Depositary Receipts granted during the year 2010 amounted to €635,790. The Fair value of a Depositary Receipt is estimated as the difference between the observable market price of the shares at the grant dates and the discounted price paid by the Depositary Receipt holder.

## 10. Financial Lease Liabilities

The Group leases certain leasehold improvement by means of finance lease:

- Agreement between BDDA and AMT regarding leasehold improvements “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 5 years. The Company has the right to cancel the lease earlier on a one-year term however, the Company will then need to repay the remaining amount of leased leasehold improvements.
- Agreement between BDDA and AMT regarding leasehold improvements “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 5 years.
- AVP asset production agreement as from June 16, 2006 until December 31, 2010. The total payment over the years by AMT is €319,000. At the end of the lease the legal ownership of these assets transfers to AMT.

Amounts in € x 1,000

	31.12.2010	31.12.2009
<b>Gross finance lease liabilities – minimum lease payments:</b>		
No later than 1 year	53	100
Later than 1 year and no later than 5 years	211	217
Later than 5 years	46	100
	<b>310</b>	<b>417</b>
Future finance charges on finance leases	(51)	(76)
<b>Present value of finance lease liabilities</b>	<b>259</b>	<b>341</b>
<b>The present value of finance lease liabilities is as follows:</b>		
No later than 1 year	38	82
Later than 1 year and no later than 5 years	176	167
Later than 5 years	45	92
	<b>259</b>	<b>341</b>

## 11. Debt to related party

On December 16, 2009 the Company entered into a convertible loan agreement with Forbion, one of its major shareholders, in respect of five-year unsecured and unsubordinated loan note bonds, which have an issue price of 100% and pay an annual coupon of 5%. This loan was drawn down on December 23, 2009. During the conversion period, which started six months after the funding date (or at the earlier occurrence of a limited number of events, such as a public offer for AMT) and which ends on the final maturity date, the Bonds are convertible into ordinary shares of AMT at an initial conversion price of €3.91, representing a conversion premium compared to AMT's share price at the date of issue of approximately 30%. The conversion price may be adjusted in the case of certain dilutive events, including an issue of shares at a discount to the average share price over the preceding 5 day. A consequence of the private placement in October 2010 (further details are given below) the conversion price of the bonds was adjusted from €3.91 per share to €3.69 per share. At 6 October 2010 such a dilutive event occurred and the conversion price was adjusted accordingly to €3.69, representing a conversion premium compared to AMT's share price at this date of 54%. During the conversion period AMT has the option to call the conversion of the Bonds if AMT's share price exceeds 150% of the then prevailing conversion price for a period of at least ten consecutive trading days. Funds managed by Forbion Capital Partners are the initial holders of the tradable loan note bonds, which have not been listed.

Further details on the accounting policy applied to the convertible loan agreement is described in paragraph 2.10 (convertible loan) above.  
The fair value of the liability part of the loan is €4,413,000.

At December 31, 2010 the conversion price of the convertible loan was above the market price of AMT ordinary shares. In such a situation the convertible loan is not regarded as being dilutive at December 31, 2010.

The valuation methodology used for the option part adopted a Black-Scholes approach on the assumption that the loan will not be converted before its maturity date.

Under IFRS 7.27, the relevant factors considered within the valuation model for the compound of the instrument are as follows:

- AMT share price of €1.88 (December 31, 2009: €3.03);
- Conversion price of €3.69 (December 31, 2009: €3.91);
- Expected life of the instrument of 4 years (December 31, 2009: 5 years);
- Annualised volatility of AMT share price of 50% (December 31, 2009 50%);
- Implied call price of €5.535 (being 150% of the €3.69 exercise price) (December 31, 2009: €5.865);
- Annual rate of quarterly dividends of 0% (December 31, 2009: 0%); and
- Discount rate – Bond yield equivalent of 1.758% (December 31, 2009: 2.637%).

The rate used in 2010 for discounting the financial liability represented by the loan element of the convertible in 2010 was 8.5% per annum. The comparative figure for 2009 has been restated on this basis. Previously the 2009 presentation assumed a discount rate of 10% per annum, leading to a different allocation of value between the loan component and the conversion right, although the overall liability for 2009 of the convertible remains unchanged.

Amounts in € x 1,000

	31.12.2010	31.12.2009
Loan component against amortised costs	4,413	4,294
Fair value of conversion right	209	429
	4,622	4,723

## 12. Trade and Other Payables

Trade and other payables are as follows:

Amounts in € x 1,000

	31.12.2010	31.12.2009
<b>Trade payables</b>	<b>1,556</b>	<b>1,182</b>
Wage taxes	129	189
Accrued social security costs	67	26
<b>Social security and other taxes</b>	<b>196</b>	<b>215</b>
Short-term lease liabilities	38	82
Accrued expenses	961	2,099
Other amounts to be paid	1,451	1,335
<b>Other current liabilities</b>	<b>2,450</b>	<b>3,516</b>

The carrying values of trade and other payables are assumed to approximate their fair values.

## 13. Revenues and Other Income

The Group's other income comprises certain subsidies, which support the Group's research efforts in defined research and development projects.

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## 14. Expenses by Nature

The research and development costs amounted to €16,404,000 and €13,241,000 in 2010 and 2009 respectively and comprise allocated employee costs, GMP facility costs, clinical development costs, collaboration costs, license costs, the costs of laboratory consumables and allocated depreciation costs. General and administrative costs amounted to €4,113,000 and €4,913,000 in 2010 and 2009 respectively and comprised allocated employee costs, office costs, consultancy costs and administrative costs.

The research and development costs and general administrative costs can be specified as follows:

Amounts in € x 1,000

		31.12.2010	31.12.2009
Employee benefit expenses	(15)	8,306	8,544
Laboratory and development expenses		6,871	5,579
Legal and advisory expenses		1,607	1,264
Office and housing expenses		1,445	1,297
Patents and licenses		926	475
Other operating expenses		677	307
Depreciation expenses	(6)	685	688
		<b>20,517</b>	<b>18,154</b>

For leases where the Group is a lessee under operating leases, lease rentals amounting to €701,000 (2009: €707,000) are included in “general and administrative costs” in the income statement.

## 15. Employee Benefits

Wages and salaries of 2009 include termination expenses incurred in respect of the retirements of former management.

Amounts in € x 1,000

		31.12.2010	31.12.2009
Wages and salaries		5,400	5,923
Social security costs		503	485
Share options and depository receipts granted to directors and employees (Note 9)		957	428
Pension costs – defined contribution plans		565	239
Other employee expenses		881	1,469
		<b>8,306</b>	<b>8,544</b>
Number of employees at the end of the period		85	83

## 16. Finance Income and Finance Costs

Amounts in € x 1,000

	31.12.2010	31.12.2009
<b>Finance income:</b>		
Interest income current accounts	252	647
Derivative results	220	–
	<b>472</b>	<b>647</b>
<b>Finance expense:</b>		
Bank borrowings-overdrafts and other debt	(7)	–
Loan from related party	(369)	–
Finance leases	(18)	(23)
<b>Exchange result</b>	<b>(127)</b>	<b>–</b>
	<b>(521)</b>	<b>(23)</b>
<b>Finance income/(costs) – net</b>	<b>(49)</b>	<b>624</b>

## 17. Corporate Income Taxes

Amounts in € x 1,000

	31.12.2010	31.12.2009
Current tax	–	–
Deferred tax	–	–
	–	–
Profit/(loss) before tax	(19,118)	(17,175)
Expenses not deductible for tax purposes	957	440
Tax losses for which no deferred income tax asset was recognized	18,161	16,735
<b>Tax charge</b>	<b>–</b>	<b>–</b>

No tax charges or income have been recognized in the years 2010 and 2009 since the company is in a loss-making position and no deferred tax asset has been recognized for carry-forward losses (also refer to the accounting policies).

As a result of changes in the Dutch income tax law, tax loss carry-forward is subject to a time limitation of nine years. Losses incurred in the years up to 2002 can still be offset against profits up to and including 2011.

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In 2009 the Group changed its policy on the treatment of tax losses, following advice that its previous policy of capitalizing R&D expenditure for fiscal purposes was unlikely to be compatible with Netherlands tax legislation. Accordingly the Company has recognized the full amount of its losses in the year in which they were incurred. As noted above, these losses need to be used within 9 years of being incurred. The total amount of tax losses carried forward amounts to €77,713,000 as per December 31, 2010 (2009: €59,552,000).

The date of expiry of these losses is summarized in the following table. In the year ended 31 December 2010 the amount of unused tax losses that expired was €nil (2009: €nil).

Amounts in € x 1,000

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Loss expiring	644	–	56	1,336	1,838	3,310	35,633	16,735	18,161

## 18. Earnings per Share

### Basic Earnings per Share

Amounts in € x 1,000

	31.12.2010	31.12.2009
Result attributable to equity holders of the Company	(19,118)	(17,175)
Weighted average number of ordinary shares	16,863	14,708
<b>Basic earnings (loss) per share (Euros per share)</b>	<b>(1.13)</b>	<b>(1.17)</b>

Basic earnings per share is calculated by dividing the profit attributable to equity holders of the Company by the weighted average number of shares outstanding during the period.

### Diluted Earnings per Share

For the periods included in these financial statements, neither the share options nor the convertible loan are included in the diluted earnings per share calculation as the Group was loss-making in all periods. Consequently basic and diluted earnings per share are the same.

## 19. Dividends per Share

The Company did not declare dividends for the years presented in these consolidated financial statements.



## 20. Cash Flow Statement

In the cash flow statement, proceeds from issuance of shares comprise:

Amounts in € x 1,000

	31.12.2010	31.12.2009
Issue of share capital	14,410	49
Expenses incurred and paid	(1,000)	–
	<b>13,410</b>	<b>49</b>

In the cash flow statement, proceeds from issuance of loans:

Amounts in € x 1,000

	31.12.2010	31.12.2009
Issuance of loan to related party (note 10)	–	5,000
Expenses incurred and paid	–	(277)
	–	<b>4,723</b>

## 21. Contingencies

### Royalties and Milestones

In the course of its business the Company enters as a licensee into contracts with other parties to obtain freedom to operate with regard to the development and marketing of its pipeline products. The Company will need to pay royalties to the licensors based on future sales levels and milestone payments whenever defined milestones will be met. As future sales levels are uncertain, as well as if and when the milestones will be met, the financial effect of these agreements cannot be estimated reliably.

### Wage Tax Audit

On January 20, 2009, the Company received an audit report from the Dutch tax authorities regarding the issuance of depository receipts to employees in 2006. The tax authorities concluded that additional wage tax should have been paid regarding this issuance, and made an additional assessment on February 10, 2009. On May 7, 2010 the Company settled the liability with the Dutch tax authorities. The settlement amount was not material to the financial position of the Company.

## 22. Commitments

### Operating Lease Commitments

The Group leases various office space and laboratory space under operating lease agreements, mainly an agreement between the Group and BDDB and AVP (Second Rental Agreement) for the lease of a building located on Meibergdreef 61 from October 1, 2005 until September 30, 2016 and an agreement for the lease of Meibergdreef 57 from July 1, 2006 until September 30, 2016. The annual lease payment amounts to € 360,000. These contracts contain an option to extend the lease by another 5 years under similar conditions.

The lease expenditure charged to the income statement during the year for operating leases amounts to € 701,000 in the year ended December 31, 2010 (2009: € 707,000). The future aggregate minimum lease payments under non-cancellable operating leases are as follows:

Amounts in € x 1,000

	31.12.2010	31.12.2009
No later than 1 year	690	698
Later than 1 year and no later than 5 years	1,455	1,719
Later than 5 years	–	426
	<b>2,145</b>	<b>2,843</b>

### Research and Development Commitments

The Group has entered into research and development commitments in relation to the Group's product pipeline. The future aggregate minimum payments under these research and development commitments are as follows:

Amounts in € x 1,000

	31.12.2010	31.12.2009
No later than 1 year	900	387
Later than 1 year and no later than 5 years	225	40
Later than 5 years	–	–
	<b>1,125</b>	<b>427</b>

### Grant Commitments

From October 1, 2000 until May 31, 2005, the Company received a grant called "Technisch ontwikkelingskrediet (TOK)" from the Dutch government. This TOK Grant includes a repayment clause in case the Company generates revenues from this project. AMT 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 January 1, 2008 through December 31, 2017 as a percentage of revenues which are derived from the sale of

AMT-011 for hyperlipoproteinemia type I. If future royalty payments are not sufficient to repay the grant on or prior to December 3, 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 December 31, 2010 was €5,352,000, comprising the original total amount of the grant together with accrued interest.

Historically, the Company also received a “Technisch ontwikkelingsproject” (TOP) grant amounting to €130,000 on a project that was terminated. If the Company realizes income from the sale of assets developed under that grant, repayment clauses will apply.

On 5 January 2010 the Company was 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 (which is expected to be demonstrated if the product can be successfully commercialised). The credit is interest-bearing at a rate of 11.4% per annum. To date we have received €729,000 under this investment credit, and at December 31, 2010 the total amount of the liability was €769,826, representing the amount of the original advance together with accrued interest. The credit 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.

## 23. Related-Party Transactions

Forbion Capital Partners has a share in the Company in excess of 10%. In addition, Professor Sander van Deventer, who served as interim CEO from 1 February–25 October 2009 and who was subsequently appointed as a member of the Supervisory Board on 28 April 2010, is a partner of Forbion Capital Partners.

Based on the information above, Forbion Capital Partners is a related party of AMT.

### Transactions

In relation to parties during the time that they were related parties to AMT.

### Expenses

In 2010:

Professor Sander van Deventer, who is retained by Forbion, a significant shareholder in the Company, served as an advisor to the company and since April, 28 2010 as a member of the Supervisory Board. Professor Sander van Deventer received a total of €293,000 in respect of his services (2009: €213,000).

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As part of the arrangements relating to the convertible loan, the Company reimbursed the legal expenses of Forbion, a significant shareholder in the Company.

These legal expenses amounted to € 20,000. In addition the coupon interest, 5%, on the convertible loan amounting to € 250,000 was paid (2009: nil). See note 11.

### Key Management Compensation

The remuneration of the Supervisory Directors amounted to € 768,000 in 2010 (2009: € 335,000) as follows:

Amounts in € x 1,000

	Salary	Bonus	Share-based payments	Pensions	Advisor's fee	2010 Total	2009 Total
Ferdinand Verdonck <sup>5</sup>	–	–	69	–	58	127	40
Philippe Van Holle	–	–	69	–	27	96	27
Sander van Deventer <sup>1</sup>	–	–	274	–	19	293	213
Joseph Feczko <sup>2</sup>	–	–	69	–	8	77	–
Steven Holtzman <sup>2</sup>	–	–	69	–	8	77	–
Francois Meyer <sup>2</sup>	–	–	69	–	8	77	–
Alexander Ribbink <sup>3</sup>	–	–	–	–	8	8	30
George Morstyn <sup>4</sup>	–	–	–	–	13	13	25
<b>Total</b>	–	–	<b>619</b>	–	<b>149</b>	<b>768</b>	<b>335</b>

<sup>1</sup> Appointed 28 April 2010

<sup>2</sup> Appointed 20 September 2010

<sup>3</sup> Resigned 28 April 2010

<sup>4</sup> Resigned 30 June 2010

<sup>5</sup> Included in the above amount is a total of € 20,000 in respect of underpayment for the years 2008 and 2009.

Amounts in € x 1,000

31.12.2010	Short term employee benefits	Share-based payments <sup>5</sup>	Post-employment benefits	Other long term benefits	Termination benefits	Total
Jörn Aldag	407	169	57	–	–	633
Piers Morgan <sup>1</sup>	208	113	19	–	–	340
Senior Management	1,019	620	123	–	–	1,762
<b>Total</b>	<b>1,634</b>	<b>902</b>	<b>199</b>	–	–	<b>2,735</b>

The total remuneration we paid to or for the benefit of members of our Board of Management and our Senior Management in 2010 amounted to approximately € 3,503,000 (2009: € 2,827,000), respectively. The tables above and below denotes the breakdown in the remuneration in 2009 of the members of the Management Board and Senior Management:

1. Mr. Morgan was appointed CFO on 1 December 2009. The Annual General Meeting of Shareholders on 28 April 2010 confirmed the appointment of Mr. Morgan to the Management Board.

Amounts in € x 1,000

31.12.2009	Short term employee benefits	Share-based payments <sup>5</sup>	Post-employment benefits	Other long term benefits	Termination benefits	Total
Ronald Lorijn <sup>1</sup>	23	–	–	–	443	466
Sander van Deventer <sup>2</sup>	213	–	–	–	–	213
Jörn Aldag <sup>3</sup>	81	314	10	–	–	405
Senior Management <sup>4</sup>	988	13	119	–	388	1,508
<b>Total</b>	<b>1,305</b>	<b>327</b>	<b>129</b>	<b>–</b>	<b>831</b>	<b>2,592</b>

<sup>1</sup> Mr. Lorijn resigned on 22 January 2009.

<sup>2</sup> Mr. van Deventer was appointed interim CEO on 1 February 2009, following the resignation of Mr. Lorijn. Mr. van Deventer was seconded to the Company by Forbion Capital Partners Management Services B.V. for a monthly fee of €11,000. On 5 October 2009, following the appointment of Mr. Aldag, Mr. van Deventer resigned from the Management Board. He continues to serve as a consultant, providing scientific advice to the Company. The Short term employee benefits represent payments as Advisor's fee.

<sup>3</sup> Mr. Aldag was appointed CEO on 5 October 2009. The Extraordinary General Meeting of Shareholders on 4 November 2009 confirmed the appointment of Mr. Aldag as a member of the Management Board. Mr. Aldag received a grant of 110,000 depositary receipts under the Company's share incentive plan.

<sup>4</sup> This amount includes certain termination payments made in respect of former members of the Senior Management Team.

<sup>5</sup> The share-based payment reflects the difference between the price subscribed for Depositary Receipts and the underlying share price at the date of grant of such Depositary Receipts, as required by IFRS 2.

#### Shares and Share Options Held by Key Management

	Number of options	Number of depositary receipts for shares	Number of shares
Jörn Aldag	131,400	110,000	29,412
Piers Morgan	87,600	–	11,765
Senior Management	503,800	28,714	–
<b>Total</b>	<b>722,800</b>	<b>138,714</b>	<b>41,177</b>

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Previously the Company had identified a proposed grant of 133,000 options over Depositary Receipts held by Jorn Aldag, Piers Morgan and certain other members of the Senior Management. Following further discussion between the Supervisory Board and the relevant employees, it was established that there was no mutual understanding between the parties as to the terms and conditions of such options. Consequently these purported 133,000 options were never validly created and the relevant employees have confirmed that they have no rights in this respect.

### Receivables and Payables Key Management

Amounts in € x 1,000

	31.12.2010	31.12.2009
Receivable Senior Management	35	34
<b>Total</b>	<b>35</b>	<b>34</b>

## 24. Auditor Services and Fees

The auditors PricewaterhouseCoopers, have performed the following services for the Company:

Amounts in € x 1,000

	31.12.2010	31.12.2009
Audit fees Annual Report	81	78
Equity offering advisory services	58	–
Audit fees halfYear Report	60	23
Tax and HR advisory services	66	47
<b>Total</b>	<b>265</b>	<b>148</b>



Company-Only Financial  
Statements

# Balance Sheet of Amsterdam Molecular Therapeutics (AMT) Holding N.V.

Amounts in € x 1,000

<b>Assets</b>			
	Note	31.12.2010	31.12.2009
<b>Non-current assets</b>			
Investments in associates	(B)	–	572
Receivables on associates	(B)	10,864	15,223
		<b>10,714</b>	<b>15,795</b>
<b>Current assets</b>			
Cash		7,416	7,338
<b>Total assets</b>		<b>18,280</b>	<b>23,133</b>
<b>Equity</b>			
Issued share capital	(C)	940	592
Share premium reserve	(C)	99,136	86,074
Other reserves	(C)	1,788	831
Retained earnings	(C)	(88,205)	(69,087)
<b>Total equity</b>		<b>13,659</b>	<b>18,410</b>
<b>Non-current liabilities</b>			
Debt to related party	(D)	4,621	4,723
<b>Total liabilities</b>		<b>4,621</b>	<b>4,723</b>
<b>Total equity and liabilities</b>		<b>18,280</b>	<b>23,133</b>

The selected Notes on pages 96 to 98 are an integral part of these company-only financial statements.



# Income Statement of Amsterdam Molecular Therapeutics (AMT) Holding N.V.

Amounts in € x 1,000

	31.12.2010	31.12.2009
Income from subsidiaries after taxes	(18,969)	(17,175)
Interest payable on related party convertible loan	(369)	–
Derivative result related party convertible loan	220	–
<b>Net result</b>	<b>(19,118)</b>	<b>(17,175)</b>

The selected Notes on pages 96 to 98 are an integral part of these company-only financial statements.

# Notes to the Company-Only Financial Statements

## A. General

The company-only financial statements are part of the 2010 financial statements of Amsterdam Molecular Therapeutics (AMT) Holding N.V.

With reference to the company-only income statement of Amsterdam Molecular Therapeutics (AMT) Holding N.V., use has been made of the exemption pursuant to Section 402 of Book 2 of the Netherlands Civil Code.

For setting the principles for the recognition and measurement of assets and liabilities and determination of the result for its company-only financial statements, Amsterdam Molecular Therapeutics (AMT) Holding N.V. makes use of the option provided in Section 2:362 (8) of the Netherlands Civil Code. These consolidated EU-IFRS financial statements are prepared according to the standards laid down by the International Accounting Standards Board and adopted by the European Union. Please see the Notes to the consolidated financial statements for a description of these principles.

In the company-only financial statements, investments in subsidiaries are stated at net asset value. The net asset value is determined on the basis of the accounting principles applied by the Company.

On June 5, 2007 Amsterdam Molecular Therapeutics (AMT) B.V. changed its name to Amsterdam Molecular Therapeutics Holding BV and transferred its intellectual property activities and other activities by means of a statutory demerger to two newly established subsidiaries Amsterdam Molecular Therapeutics (AMT) IP B.V. and Amsterdam Molecular Therapeutics (AMT) B.V.

On June 20, 2007 Amsterdam Molecular Therapeutics (AMT) Holding B.V. converted to the public company Amsterdam Molecular Therapeutics (AMT) Holding N.V.

## B. Investments in Subsidiaries

Amsterdam Molecular Therapeutics (AMT) Holding N.V. holds the following subsidiaries:

Name	Percentage of shares owned	Statutory seat
Amsterdam Molecular Therapeutics (AMT) B.V.	100%	Amsterdam
Amsterdam Molecular Therapeutics (AMT) IP B.V.	100%	Amsterdam

Amounts in € x 1,000

	31.12.2010	31.12.2009
Beginning of the year	572	572
Movement for the year	(572)	–
<b>End of the year</b>	<b>–</b>	<b>572</b>
Amsterdam MolecularTherapeutics (AMT) B.V.	–	–
Amsterdam MolecularTherapeutics (AMT) IP B.V.	–	572
<b>End of the year</b>	<b>–</b>	<b>572</b>

The comparisons changed as a result of the methodology of presentation. The Net asset value of the group companies and long term intercompany receivables are shown separately, see also note C.

The company is showing the convertible loan from Forbian which effects the receivables on group companies.

In the event the group company has a negative net equity value the group company will be shown as nil. The difference between the negative net equity value and the value shown will be deducted from the group receivable of the respective group company.

## C. Amounts due from Group Companies

Amounts due from group companies reflect the receivables on these companies adjusted for the amount that would be otherwise stated as the negative net asset value of the individual group company.

Amounts in € x 1,000

	31.12.2010	31.12.2009
Beginning of the year	15,223	32,398
Movement for the year	(4,359)	(17,175)
<b>End of the year</b>	<b>10,864</b>	<b>15,223</b>
Amsterdam MolecularTherapeutics (AMT) B.V.	10,675	14,944
Amsterdam MolecularTherapeutics (AMT) IP B.V.	189	279
<b>End of the year</b>	<b>10,864</b>	<b>15,223</b>

## D. Shareholders' Equity

There is no difference between equity according to the Company balance sheet and equity according to the consolidated balance sheet. For details of the movements in and components of equity, reference is made to the "Statement of changes in equity" and Note 9 of the consolidated financial statements.

## E. Amounts due to Related Parties

In December 2009 the Company issued convertible loan notes as described in the consolidated financial statements, including Notes 2, 4 and 11 to the consolidated financial statements.

## F. Remuneration of Directors and Supervisory Directors

The remuneration of the Supervisory Directors amounts to €789,000 (2009: €132,000). For further details, reference is made to Note [23] of the consolidated financial statements.

The total remuneration we paid to or for the benefit of members of our statutory Board of Management in 2010 amounted to approximately €973,000. For further details, reference is made to Note [23] of the consolidated financial statements.

## G. Signing of the Financial Statements

Amsterdam, March 4, 2011.

Statutory and Supervisory Directors

### Statutory Directors

Jörn Aldag, Chief Executive Officer  
Piers Morgan, Chief Financial Officer

### Supervisory Directors

F.L.J. Verdonck, Chairman  
P.M.M.J. van Holle, Member  
S.J.H. van Deventer, Member  
Dr. J.M. Feczko, Member  
S.H. Holtzman, Member  
F. Meyer, Member



# Independent Auditor's Report to the General Meeting of Shareholders of Amsterdam Molecular Therapeutics (AMT) Holding N.V.

## Auditors Report. Report on the Financial Statements

We have audited the accompanying financial statements 2010 of Amsterdam Molecular Therapeutics (AMT) Holding N.V., Amsterdam. The financial statements include the consolidated financial statements and the company financial statements. The consolidated financial statements comprise the consolidated balance sheet as at 31 December 2010, the consolidated income statement, the statements of comprehensive income, changes in equity and cash flows for the year then ended and the notes, comprising a summary of significant accounting policies and other explanatory information. The company financial statements comprise the company balance sheet as at 31 December 2010, the company income statement for the year then ended and the notes, comprising a summary of accounting policies and other explanatory information.

## Management Board's Responsibility

The Management Board is responsible for the preparation and fair presentation of these financial statements in accordance with International Financial Reporting Standards as adopted by the European Union and with Part 9 of Book 2 of the Dutch Civil Code, and for the preparation of the management board report in accordance with Part 9 of Book 2 of the Dutch Civil Code. Furthermore, the Management Board is responsible for such internal control as it determines is necessary to enable the preparation of the financial statements that are free from material misstatement, whether due to fraud or error.

## Auditor's Responsibility

Our responsibility is to express an opinion on these financial statements based on our audit. We conducted our audit in accordance with Dutch law, including the Dutch Standards on Auditing. This requires that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the company's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the company's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by the management board, as well as evaluating the overall presentation of the financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

### **Opinion with Respect to the Consolidated Financial Statements**

In our opinion, the consolidated financial statements give a true and fair view of the financial position of Amsterdam Molecular Therapeutics (AMT) Holding N.V. as at 31 December 2010, and of its result and its cash flows for the year then ended in accordance with International Financial Reporting Standards as adopted by the European Union and with Part 9 of Book 2 of the Dutch Civil Code.

### **Opinion with Respect to the Company Financial Statements**

In our opinion, the company financial statements give a true and fair view of the financial position of Amsterdam Molecular Therapeutics (AMT) Holding N.V. as at 31 December 2010, and of its result for the year then ended in accordance with Part 9 of Book 2 of the Dutch Civil Code.

### **Emphasis of Uncertainty with Respect to the Going Concern Assumption**

We draw attention to note 2.1 to the consolidated financial statements which indicates that the company does not have sufficient cash resources to fully cover the projected expenditure over the coming 12 months. This condition, along with other matters as set forth in note 2.1, indicates the existence of a material uncertainty which may cast significant doubt about the company's ability to continue as a going concern. Our opinion is not qualified in respect of this matter.

### **Report on other Legal and Regulatory Requirements**

Pursuant to the legal requirement under Section 2: 393 sub 5 at e and f of the Dutch Civil Code, we have no deficiencies to report as a result of our examination whether the management board report, to the extent we can assess, has been prepared in accordance with Part 9 of Book 2 of this Code, and whether the information as required under Section 2: 392 sub 1 at b-h has been annexed. Further we report that the management board report, to the extent we can assess, is consistent with the financial statements as required by Section 2: 391 sub 4 of the Dutch Civil Code.

Amsterdam, 4 March 2011  
PricewaterhouseCoopers Accountants N.V.

A.C.M. van der Linden RA

Other Information

## Statutory Arrangement Concerning the Appropriation of Profit

The statutory arrangements regarding the appropriation of the profit is described in article 33 of the articles of association:

33.1 Each year, the Executive Board may, subject to the approval of the Supervisory Board, determine which part of the profits shall be reserved.

33.2 The part of the profit remaining after reservation in accordance with Article 33.1 shall be distributed as dividend on the Shares.

33.3 Distributions may be made only up to an amount which does not exceed the amount of Distributable Equity.

33.4 Distribution of profits shall be made after adoption of the annual accounts if permissible under the law given the contents of the annual accounts.

33.5 The Executive Board may resolve to distribute interim dividends on the Shares. Such resolution shall be subject to the approval of the Supervisory Board.

33.6 In calculating the amount of any distribution on Shares, Shares held by the Company shall be disregarded.

33.7 The sections 2:103, 2:104 and 2:105 of the Dutch Civil code shall apply to the distributions to holders of Shares.

## Proposed Result Appropriation for the Financial Year 2010

The General Meeting of Shareholders will be proposed to debit retained earnings with the loss for 2010 of €19,118,000.

## Events after the Balance Sheet Date

Since the balance sheet date there have been no events which fall to be disclosed.



# Gene Therapy Opportunity

## Gene Therapy Opportunity

# Gene Therapy Opportunity

AMT has established a safe and effective gene delivery approach and a unique process that enables the economical, commercially scalable manufacturing of gene therapy products. This powerful platform combined with the research expertise of our collaboration partners provides AMT with exciting opportunities to deliver more curative therapies to patients faster.

“There is an urgent need for a long-term solution, for cure of rare and serious diseases.”

For a large number of serious illnesses today there is no lasting solution nor cure available which addresses the cause of the problems. Existing therapies are limited to symptomatic treatment at best. 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 illnesses caused by damaged or faulty genes. This technique offers the potential for a long-term or even life-long cure. Today, most gene therapy studies are aimed at cancer, and at orphan diseases; orphan diseases are those that are both rare (US: fewer than 200,000 people afflicted; EU: fewer than 5 per 10,000 population afflicted) and life threatening. Between 5,000 and 8,000 orphan diseases have been identified to date, 80% of which are believed to be caused by a single gene defect.

“Gene therapy is likely to be most successful with diseases caused by single gene defects.”

Genes themselves do not actually do anything. They serve as the blueprint that the body’s cellular machinery uses 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 blood clotting will not happen at times when it’s 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 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 the relevant protein. AMT’s Parkinson disease project is an example hereof.

“The combination of novel technologies together with growing understanding and experience are showing that gene therapy can be safe and effective.”

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, to date only one gene therapy product has ever been approved for sale, and that solely in China. In general, gene therapy is highly innovative and still in 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.

AMT is now leading the field of gene therapy companies competing to bring safe and efficacious medications to commercialization. We have developed a broad platform that has helped to overcome the major challenges which the gene therapy industry was facing. The following key technologies clearly differentiate our approach from other gene delivery systems.

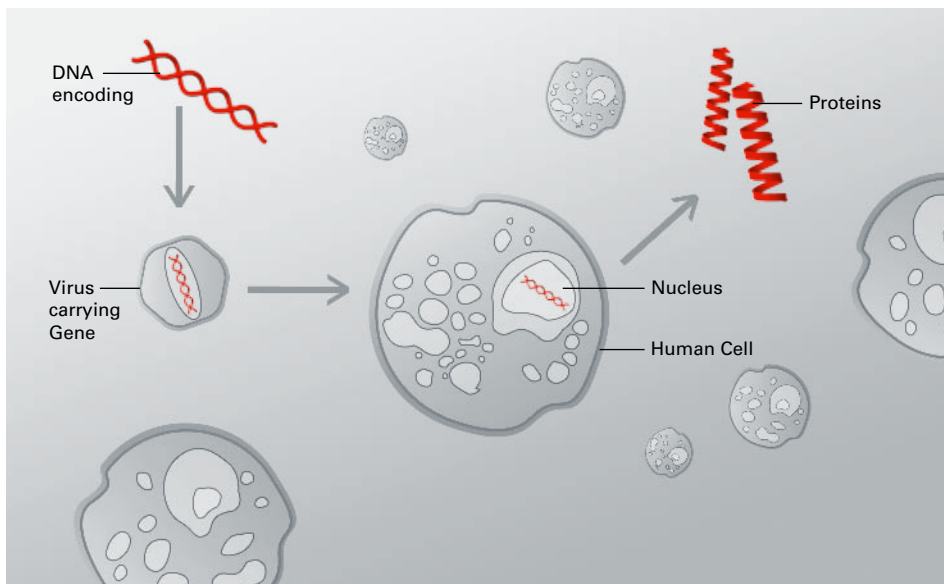
# Introducing the AMT Approach

## Promising Vector Technology

### AMT Offers the Potential for a Safe and Effective Gene Delivery Solution

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 insert the gene in the nucleus. All our gene therapy products are based around Adeno Associated Virus (AAV) vector technology. AAV vectors are generally considered safe and have been tested in over 40 clinical trials to date. “Wild type”, naturally occurring AAVs are non-pathogenic and do not in themselves cause disease in humans. AMT “strips” the naturally occurring AAV before using it as vector to carry the therapeutic genes, and through this ensures that the vector used cannot replicate anymore. The genes contained in wild type and AMT-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. non-integrated) gene form is created, 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 effectively eliminates the risk of inducing cancer, a risk seen with 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, and AAV can be used to target both dividing and non-dividing cells. Other gene therapy platforms cannot “infect” non-dividing cells. Targeting non-dividing cells/tissues has the added advantage of limiting loss of activity of gene therapy from loss of cells with good genes in them, and we make use of this. Our experience with our lead gene therapy product, Glybera®, has clearly demonstrated that our technology provides multi-year tissue-targeted expression of the therapeutic protein after one-time administration.



## Unique Manufacturing Process

### **Economically Feasible and Commercially Scalable Manufacturing Technology**

In the past, the production of gene therapy products, especially AAV-based vectors, has been hampered by the challenges of scaling-up commercial production (traditionally carried out in mammalian cells) in an economic way; to date this challenge still represents a major obstacle. We have succeeded in developing a proprietary new platform manufacturing technology that allows safe, effective, cGMP (pharmaceutical quality standard) compliant, economically feasible and commercially scalable manufacturing of our products – a major differentiating factor in gene therapy. Our novel approach is based on the use of a combination of baculovirus and insect cells. It is highly flexible so that the process 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 can undertake full development and commercial-scale manufacturing, as shown by our lead product Glybera®.

## Proven Clinical Development and Regulatory Expertise

### **The Filing of Glybera® has Uniquely Demonstrated AMT's Leading Capabilities**

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. The major hurdles for those organizations are their clinical development and regulatory capabilities. Regulatory authorities are concerned over the low number of patients included in clinical trials, the way studies have been carried out and insufficient information on the safety of individual products which makes it difficult to interpret the results.

AMT has all the necessary skills to advance a product through all stages of clinical development and to round off regulatory processes to filing. The Company has also established close links to the regulatory bodies and seeks early discussions at all stages of development to ensure that its trials are in conformity with legal and ethical requirements. In developing and filing Glybera®, AMT has managed the entire process without the support of a big partner, a substantial achievement. This proven capability has made already AMT an attractive fit for a number of academic institutions with exciting early stage programs to enter into a collaboration with AMT.

## Modular Platform, Focused Approach

### How AMT Taps the Broad Potential of its Capabilities

Using our 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. Our current pipeline is focused on a few programs which are either for orphan diseases or for more common illnesses in which breakthrough innovation can fundamentally change therapeutic paradigms. Both targeted disease areas share a high unmet medical need. Our technology offers the possibility of faster development times, lower cost of development and the unmet needs are associated with lower marketing costs. Examples of the first group are our lead product Glybera®, now in registration, Porphyria and Duchenne. The latter group includes Hemophilia and Parkinson's disease. In line with this two-tiered approach, AMT has implemented a business model combining proprietary and partnered development of its products in order to retain value and conserve cash.

"We focus our research on programs with either a low cost of development or a high chance of successful early partnering. This balance is fundamental to our future corporate and commercial success."

## Strategic Partnerships

### How Partnerships Help AMT Fueling its Pipeline and Balancing Development Risk

We believe that based on recent successes such as Glybera®s there is now increasing demand for gene therapies. There seems to be a growing number of opportunities for partnerships – in-licensing of disease-modifying genes on the one side, and out-licensing programs on the other. Our agreements with CIMA/Digna Biotech in Spain and with St Jude Children's Hospital in Memphis, USA, give AMT access to cutting edge medical research. We leverage the preclinical work and expertise of our strategic partners in many orphan diseases and combine this with our proprietary gene delivery and manufacturing platform and clinical development capabilities to balance risks and reduce time-to-market significantly.

"Combining our unique platform with research of strategic partners provides us with significant opportunities to fuel our pipeline while reducing risk."

## Fast Development

### 5–8 Years, Compared to 10–15 Years Traditionally

Gene therapy development can be dramatically accelerated: Clinical trials with gene therapy start in patients, not in healthy subjects. The first clinical studies aimed at demonstrating safety thus will also provide early signs of efficacy. Once a vector has been studied and accepted for use in humans, it is likely that that same vector can be reapplied in future in another disease area and product, with a new therapeutic gene incorporated. Assessment of the safety of such a new product can be concentrated on the new gene product (protein) itself rather than on the already known vector, and hence overall new product development may be significantly accelerated. Regulatory authorities may also become more familiar

"Our partnership model, our modular platform and our focus on orphan diseases allow us to bring drugs to patients faster."

**Gene Therapy Opportunity**  
Introducing the AMT Approach

with our approach, understand the modularity of our platform and may require less data to be obtained for regulatory approval. This should allow us to further reduce development time.

Our focus on orphan diseases is another important aspect. The regulatory frameworks in the EU and the US encourage research into, and development of, orphan drugs in order to better serve patients suffering from rare diseases (see “Roadmap 2015” of the European Medicines Agency). This is being addressed by longer market exclusivity periods, pre-approval compassionate use (allowing certain patients access to drugs before regulatory approval is granted), reduced fees, and research grants. In addition, the approval of orphan drugs involves pivotal trials that consist of a limited number of patients (potentially only 10–100), and a fast track approval process was introduced to allow drugs fulfilling high unmet medical needs to get to market more quickly than conventional drugs.

## ... to the Benefit of Patients and Investors

AMT is now well positioned to address the urgent needs of many patients suffering from diseases for which no or suboptimal therapeutic solutions exist today. Many, but not all of these diseases are rare, are “orphans”. People affected by these diseases have little prospect of seeing a novel therapy because current drug development processes require too much time and resources to provide pharmaceutical companies with a sufficient return on their investment. Gene therapy, and the flexibility of AMT’s platform, offer the hope of bringing more curative or causal therapies to patients faster. Furthermore, although orphan drugs target a smaller patient population than non-orphan drugs, “rare” is a relative term. In the United States alone, according to the National Institutes of Health (NIH) as many as 25 million people are affected by one of the 5,000 orphan disease currently diagnosed. This makes orphan diseases – and finding real therapeutic solutions for them – a serious public health concern.

Over the past decade it has become obvious that developing safe and efficacious therapies for orphans may also lead to substantial revenue generation. The best selling drug developed for an orphan indication is Erythropoietin (EPO). EPO has been subsequently expanded to target a number of indications, and in 2008 Amgen sold \$5.6 billion of EPO products.

Gene therapy is coming of age, offering hope to millions of patients, and offering opportunities for those eager to invest in innovation for health.

# Genes and Gene Therapy

## What is DNA?

Deoxyribonucleic acid (DNA) is a nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms and some viruses. The main role of DNA molecules is the long-term storage of information. DNA is often compared to a set of blueprints or a recipe, or a code, since it contains the instructions needed to construct other components of cells, such as proteins. The DNA segments that carry this genetic information are called genes, but other DNA sequences have structural purposes, or are involved in regulating the use of this genetic information.

## What are Chromosomes?

A chromosome is a singular piece of DNA, which contains many genes, regulatory and other elements. Chromosomes also contain DNA-bound proteins, which serve to package the DNA and control its functions. Chromosomes are found inside the nucleus of cells.

## What is a Gene?

A gene is the basic unit of hereditary information in a living organism. It provides the code for living organisms' traits, characteristics, functioning, and physical development. Man has around 30,000 genes that are located on 46 chromosomes.

## What are Proteins?

Proteins are large organic compounds made of amino acids. They are involved in many processes within cells. Proteins act as building blocks, or function as enzymes and are important in "communication" among cells. Proteins are an essential part of our diet.

## What is Gene Therapy?

Gene therapy is a technique for correcting defective or missing genes that cause a disease. This can be done by inserting a correctly functioning gene into the cells of the patient, so that the cells will regain proper function. Gene therapy can also be used to prevent faulty parts of a gene being used ("gene silencing") and it is possible to switch genes "on" or "off". Until now, gene therapy has mainly been researched for treatment of hereditary diseases and cancers. Scientists are also looking into the possibilities for using gene therapy for other diseases, like cardiovascular diseases, liver diseases, and Parkinson's disease. Special carriers, called vectors, are necessary to ensure that the gene will be delivered to the right cell or organ. Currently, the most common vectors are derived from viruses that have been altered to ensure that they safely and exclusively deliver a gene to the right target cell. Some technologies, including AMT's AAV platform, enable long-term expression of therapeutic genes.

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