



## Amsterdam Molecular Therapeutics Reports Half-Year Results 2011

Amsterdam, The Netherlands – August 25, 2011 – Amsterdam Molecular Therapeutics (Euronext: AMT), a leader in the field of human gene therapy, today reported its results for the first half year of 2011.

### Highlights

- Glybera®:
  - Data showing Glybera produces significant reduction in risk of pancreatitis in LPLD patients presented at European Atherosclerosis Society Meeting
  - CHMP does not consider Glybera approvable at this time
  - Chylomicrons now validated as biomarker for Glybera efficacy; data presented at American Society of Gene and Cell Therapy annual meeting
  - AMT generating further chylomicron data from existing treated patients to support re-examination process
  - Submitted for re-examination, outcome expected before end 2011
- Collaboration with Institut Pasteur-led Consortium to develop Sanfilippo B gene therapy product for cGMP manufactured material; worth up to € 1.8 million to AMT
- € 1.1 million funding for Acute Intermittent Porphyria gene therapy product as part of EU Consortium
- Grant from Dutch Parents Association for Duchenne Muscular Dystrophy gene therapy
- Appointment of Dr. Carlos R. Camozzi as Chief Medical Officer
- Key financial figures in line with guidance
- Cash & cash equivalents of € 9.1 million at June 30, 2011, in line with budget

"We have moved quickly and have already filed an application for re-examination of Glybera, after the initial disappointment with the CHMP opinion in June. We are continuing to collect more data to show that there is a long-term reduction in the incidence of pancreatitis in treated patients. We will be able to generate the additional data required from the existing treated patients, and the data will come from a trial which we had already planned to do as a post-marketing study," noted Jörn Aldag, CEO of Amsterdam Molecular Therapeutics. "AMT will also continue development of other gene therapy products in the company's pipeline."

### Operations

#### **Glybera for Lipoprotein Lipase Deficiency**

AMT has developed Glybera for the treatment of Lipoprotein Lipase Deficiency (LPLD), a rare and very severe disease. In patients with mutations in the LPL gene, dietary fat (triglyceride molecules) cannot be broken down and so causes chylomicrons, which carry triglycerides around the body, to accumulate in the blood. This may result in recurrent extremely painful and life-threatening episodes of pancreatitis. Pancreatitis, or inflammation of the pancreas, is a major clinical symptom of LPLD. It causes severe abdominal pain and often leads to hospitalization of patients as well as other complications such as diabetes and early atherosclerosis.

AMT submitted the Marketing Authorisation Application (MAA) for Glybera in December 2009; in June 2011 the CHMP published its opinion that Glybera is not approvable at this time.



Since originally submitting the MAA, AMT has generated significant additional data, including results from a long-term efficacy study of Glybera showing that improved chylomicron metabolism could be used as a biomarker for increased LPL activity in those patients missing the gene that produces this protein. Data showed that breakdown of chylomicrons produced after meals was greatly and significantly improved at both 14 and 52 weeks following one-time Glybera administration.

It was also shown that Glybera significantly reduces the risk of pancreatitis in LPLD patients. By reducing the incidence of pancreatitis episodes substantially, Glybera has the potential to help “normalize” the day to day lives of patients affected by this disease and prevent the often frequent trips to hospital that patients otherwise experience.

AMT has filed for re-examination of the Glybera MAA. This process will be completed by the end of 2011.

### **Other programs**

AMT has taken steps to bring in non-dilutive financing to cover some or all of the costs associated with its remaining programs, in order to reduce its cash expenditure.

### **Hemophilia B**

AMT continues to work with St Jude’s Children’s Hospital in the USA, which is currently financing and conducting a clinical study in US and UK. Initial results are promising, with patients showing stable and persistent expression of the Factor IX clotting protein, and able to reduce or stop their administrations of protein replacement therapy, which is the current standard of care and requires intravenous infusion up to three times per week.

By contrast, the hemophilia B gene therapy requires a single administration to provide lasting benefit – the earliest patient was treated almost 18 months ago and so far has shown no detectable lessening of the benefit from this treatment. This is the second gene therapy program AMT is involved with to show clinical benefit from a single treatment and establishes AMT as the leading gene therapy company worldwide.

### **Acute Intermittent Porphyria**

This program, in collaboration with the University of Navarra and Digna Biotech in Spain, is making encouraging progress. Earlier this year, the consortium won a significant EU grant worth approximately €1 million to AMT, which covers the majority of AMT’s expenditure at this time for this program.

In August 2011, the consortium began enrolling patients into a pre-observation study. This initial study will provide baseline data for the subsequent treatment study, which involves administering patients with a one-time gene therapy and is expected to begin in 2012.

### **Duchenne Muscular Dystrophy**

AMT is making good progress in delivery of gene therapy product to the heart. Heart failure is one of the main causes of death in Duchenne patients. The Company has also won support from the Duchenne Parents Association and continues to work with them to progress this program through pre-clinical evaluation, in addition to the ongoing support from Agentschap NL (formerly SenterNovem).

### **GDNF**

AMT is conducting pre-clinical research and has successfully completed a proof of concept study in a disease model of Parkinson’s disease in collaboration with the University of Lund, Sweden. Data generated



for AMT by the University of Wisconsin (USA) in a further pilot study using large animals also showed effective delivery, distribution and expression at levels that are expected to correlate with clinical efficacy; overcoming these challenges is one of the major challenges to clinical development. Taken together, these positive data encourage us to continue with the development of GDNF gene therapy and to extend it to other neurodegenerative indications such as multiple system atrophy (MSA) and Huntington's disease.

### **Sanfilippo B**

Under an agreement signed at the beginning of this year, AMT is collaborating with a consortium led by Institut Pasteur in the clinical development of a novel gene therapy to treat Sanfilippo B. This rare genetic disease affecting new-born children leads to progressive neuronal degeneration and death. There is no approved therapy currently available.

On behalf of the Consortium, Institut Pasteur will lead the development program and will also sponsor the initial Phase I/II clinical study. AMT will manufacture and supply the adeno-associated virus, serotype 5 (AAV5) gene therapy product to the Consortium. The overall manufacturing contract entails payments to AMT of € 1.8 million. 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 in 2012.

### **Other Research and Development**

AMT has demonstrated the advantage of its AAV vector delivery technology for the efficient delivery of short and micro RNA to inhibit disease by RNA interference in two further pre-clinical disease models, for hypercholesterolemia and Huntington's disease. RNAi-based therapeutic strategies are considered highly promising in the industry, but so far, effective delivery has been elusive. In Huntington's disease, progress is being made quickly through in vivo studies and we anticipate proof of concept data in animal models by the end of 2011 for this indication. Two other important research projects are intended to greatly enhance the value of AMT's platform: gene expression control and re-administration.

### **Other Business Activities**

The Supervisory Board, Management Board and other members of the management team have demonstrated their confidence in the prospects for AMT's success by taking a significant, fixed proportion of their remuneration in new AMT shares for the period from 1 July – 31 December 2011, and by making direct investments in AMT shares.

### **Financials**

#### **Results comparison**

Total net loss for the period ended June 30, 2011 amounted to € 8.7 million, a reduction of 7% compared to the net loss for the period ended June 30, 2010 which amounted to € 9.4 million.

Other income, mainly representing grants, increased to € 1.3 million, compared to € 0.6 million in the corresponding period to 30 June 2010. This increase reflects the Company's success in securing additional non-dilutive funding towards the costs of its programs.

The main item within operating costs reflects the investment in Glybera® to support the registration process. Development of our other development projects has been reduced as we are constrained by our current resources and are focusing on the successful completion of the Glybera registration process. Research and



development costs amounted to € 8.2 million for the period ended June 30, 2011 compared to € 8.1 million in the same period of 2010. At the same time, general and administrative costs amounted to € 1.8 million in the period ended June 30, 2011 compared to € 1.8 million in the same period of 2010.

Net interest income/(cost) amounted to € 0.0 million for the period ended June 30, 2011, consistent with the € (0.0) million in the same period in 2010.

Cash and cash equivalents amounted to € 9.1 million at June 30, 2011, a decrease of € 8.8 million compared to € 17.9 million at December 31, 2010. The decrease in cash and cash equivalents mainly stems from the operational cash outflow which amounted to € 8.8 million for the period ended June 30, 2011 (compared to an operating cash outflow of € 8.9 million for the period ended June 30, 2010).

### **Outlook**

The Company's expenditure is expected to reduce in the second half of 2011 as the Company takes steps to extend its cash position into 2012. As AMT has not yet reached the point of generating significant revenues that could fund operations, we continue to explore additional opportunities for funding, including non-dilutive sources, such as grants, and collaborations with partners; AMT also tracks opportunities for raising additional capital in conjunction with its bankers.

### **Conference call and webcast presentation**

AMT will conduct a conference call open to the public today at 3.30 p.m. CET, which will also be webcast. Netherlands dial in: +31 (0)20 707 5503; US dial in: +1 718 247 0884; UK dial in: +44 (0)20 7136 6285. Confirmation Code: 5149966

To listen to the conference call live via the internet, visit the investor relations portion of the AMT website at [www.amtbiopharma.com](http://www.amtbiopharma.com). Please go to the website 15 minutes prior to the call to register, download and install the necessary audio software.

The archived webcast also will be available for replay shortly after the close of the call.

### **About Amsterdam Molecular Therapeutics**

AMT is a leader in the development of human gene based therapies. Using adeno-associated viral (AAV) derived vectors as the delivery vehicle of choice for therapeutic genes, the company has been able to design and validate what is probably the first stable and scalable AAV production platform. This proprietary platform can be applied to a large number of rare (orphan) diseases that are caused by one faulty gene. Currently, AMT has a product pipeline with several AAV-based gene therapy products in LPLD, Hemophilia B, Duchenne Muscular Dystrophy, Acute Intermittent Porphyria, and Parkinson's Disease at different stages of research or development. AMT was founded in 1998 and is based in Amsterdam.

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For further enquiries:

Jörn Aldag

CEO

AMT

Tel : +31 20 566 7394

[j.aldag@amtbiopharma.com](mailto:j.aldag@amtbiopharma.com)

Mike Sinclair

Partner

Halsin Partners

Tel : +44 20 7318 2955

[msinclair@halsin.com](mailto:msinclair@halsin.com)



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