

## PRESS RELEASE

### APEPTICO completes €3 million financing round

**05<sup>th</sup> August, 2010, Vienna, Austria: APEPTICO Forschung und Entwicklung GmbH, a biotechnology company developing novel peptide-based drugs, today announced completion of a €3 million financing round. This equity financing combined existing and new investors from Germany and Switzerland. As an integral part of the financing round, APEPTICO will receive a €1.2 million research grant from the Austrian Research Promotion Agency (FFG).**

This €3 million financing round is equally shared by institutional Venture Capital companies (The BioScience Ventures Group AG and V+ GmbH & Co Fonds 2 KG) and business angels from Germany and Switzerland.

APEPTICO's lead products are synthetic peptides that convert structural elements of the human Tumor Necrosis Factor alpha into efficient, safe and new medicines. APEPTICO's target indications include treatment of Acute Lung Injury/Acute Respiratory Distress Syndrome, treatment of severe microbial and viral lung infections, lung transplantation and solid organ dysfunction.

The funds from the financing will be used to perform a Phase 1 clinical assessment of APEPTICO's lead peptide AP301 which has been shown to activate lung oedema reabsorption and protects both endothelial and epithelial lung cells from virulence factor- and reactive oxygen species-induced hyper-permeability of lung capillaries.

Dr. Bernhard Fischer, CEO of APEPTICO commented: "We are delighted to have secured our second equity financing with an international syndicate of venture capital and private investors. Based on the first financing round from May 2009, we completed the pre-clinical development program of our lead peptide AP301 and discovered even more peptides with improved properties. This new €3 million financing enables us to immediately initiate the early clinical development and to work on additional peptides and clinical indications."

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#### Notes to Editors:

##### About APEPTICO GmbH

APEPTICO is a privately-held biotechnology company based in Austria, developing peptide-based products targeting chronic and life-threatening diseases. The peptide molecules correspond to validated, pharmacodynamic active structures and domains of well-known proteins and biopharmaceuticals. By concentrating on synthetically produced protein structures APEPTICO avoids any risk of transmitting microbial and viral infections. Development cost and time to market are significantly reduced if compared to the recombinant development process of biomolecules. APEPTICO's development platform PEPBASE™ combines structural, functional and clinical data from relevant biopharmaceuticals and well-characterised proteins. Based on preclinical and clinical data, including adverse reactions, risk factors and contraindications to be circumvented and supported by structural, biochemical and physicochemical data, for each relevant protein a specific profile is established that links biological & functional properties with discrete structural elements.

### About AP301

AP301 is a synthetic peptide that corresponds to a structural motif of the human Tumour Necrosis Factor alpha. It is water soluble and can be administered into the lung by instillation or by inhalation. Formulated AP301 can be nebulised and the resulting aerosol is composed of peptide/water droplets of diameter 4 µm or less. AP301 was originally designed for the treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome. Additional research demonstrated that AP301 has additional significant potential in related clinical indications, such as prevention and treatment of pulmonary permeability oedema, prevention of progression of acute hypoxemic respiratory failure due to bacterial/viral pneumonia and prevention of ischemia reperfusion injury. AP301 activates lung oedema reabsorption and protects both endothelial and epithelial lung cells from virulence factor- and reactive oxygen species-induced hyper-permeability of lung capillaries. AP301 has received Orphan Drug Designation by the EMEA (European Community) for the treatment of Acute Lung Injury and by the FDA (USA) for the prevention of ischemia reperfusion injury in the lung during lung transplantation”.

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## PRESS RELEASE

### **APEPTICO's lead molecule AP301 has been validated in an experimental lung transplantation model**

**23<sup>rd</sup> February, 2010, Vienna, Austria: APEPTICO Forschung und Entwicklung GmbH, a biotechnology company developing novel peptide-based drugs, today announced that its lead molecule AP301 has been validated in an experimental lung transplantation model where intratracheal application of AP301 dramatically improved oxygenation after lung transplantation.**

APEPTICO's AP301 is a 17-amino acid cyclic peptide representing the "TIP-motif" of the human cytokine tumour necrosis factor. The international leading journal *Critical Care Medicine* has published in its latest issue (No. 38(3), pp.871-878) the article "The lectin-like domain of tumor necrosis factor improves lung function after rat lung transplantation - potential role for a reduction in reactive oxygen species generation" by Dr. Jürg Hamacher et al. This study was a collaboration between Prof. Dr. Rudolf Lucas from the Medical College of Georgia, the inventor of the TIP peptide and the University Hospital Bern, Switzerland. The results from this study, featured in the Editorial of the same issue, demonstrate that in a left lung transplantation model in rats, accompanied by ischemia reperfusion injury, endothelial hyperpermeability and Permeability Oedema which ensuing dramatically reduced oxygenation, APEPTICO's AP301 dramatically improves oxygenation (assessed by the PaO<sub>2</sub>/FIO<sub>2</sub> ratio) 24 h after lung transplantation. AP301 accomplishes this by significantly decreasing the production of reactive oxygen species and by reducing neutrophil sequestration in the lung, thus mitigating the secondary effects of reoxygenation and reperfusion.

Dr. Bernhard Fischer, CEO of APEPTICO commented: "We are very happy about these results and that this extraordinary study was high lighted by an Editorial Comment in the *Critical Care Medicine* journal with the words »the study takes us a step closer in developing therapeutic measures to combat Acute Lung Injury and various forms of Adult Respiratory Distress Syndrome«. (Critical Care Medicine (2010), 38(3), 997-998).

Prof. Dr. Rudolf Lucas, CSO of APEPTICO added: "These studies clearly demonstrate a therapeutic potential of the AP301 compound and will pave the way towards testing the compound also in more chronic models of lung transplantation as well as in other organ models of ischemia-reperfusion damage".

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### About Lung Transplantation and Primary Graft Dysfunction

Primary Graft Dysfunction (PGD), a clinical variant of Acute Lung Injury (ALI), is an important complication of lung transplantation in the immediate postoperative period. Based on the recommendations of the International Society for Heart and Lung Transplantation, PGD is currently graded based on PaO<sub>2</sub>/ FIO<sub>2</sub> ratio and chest infiltrates evaluated at various time points up to 72 hrs after transplantation. PGD occurs in approximately 10% to 25% of recipients and is the leading cause of morbidity and death in the early posttransplant period. Furthermore, PGD has important long-term consequences decreasing performance status and increasing the risk of bronchiolitis obliterans syndrome. Increased pulmonary alveolar capillary permeability associated with impaired clearing of alveolar fluid is the ultimate pathophysiological mechanism contributing to PGD, as in many other types of ALI and Adult Respiratory Distress Syndrome

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## PRESS RELEASE

### **APEPTICO granted Orphan Drug Designation by FDA for development compound AP301**

**10<sup>th</sup> February, 2010, Vienna, Austria: APEPTICO Forschung und Entwicklung GmbH, a biotechnology company developing novel peptide-based drugs, today announced that it has received Orphan Drug Designation in the USA from the Food and Drug Administration (FDA) for APEPTICO's development compound AP301. AP301 has been granted Orphan Drug Designation in the USA for "prevention of ischemia reperfusion injury in the lung during lung transplantation".**

APEPTICO's AP301 is a 17 amino acids cyclic peptide. It represents "TIP-motif" of the human tumour necrosis factor alpha. Upon pulmonary application the AP301 peptide exerts a favourable effect on lung function and decreased alveolar infiltration in the setting of ischemia reperfusion injury associated with lung transplantation. Intratracheally administered AP301 peptide leads to a major improvement of gas exchange and a diminished neutrophil count in the bronchoalveolar fluid.

Dr. Bernhard Fischer, CEO of APEPTICO commented: "I am pleased that the FDA has approved the Orphan Drug Designation for AP301 for the prevention of ischemia reperfusion injury in the lung during lung transplantation. This encouraging step builds on the announcement by the EMEA in July 2009 of granting of Orphan Medicinal Product Designation for AP301 in the EU for "treatment of acute lung injury". There remains a real unmet medical need for innovative products that work to prevent ischemia reperfusion injury that is very frequent experienced following solid organ transplants. There are no products currently authorized in the US to prevent ischemia reperfusion injury during lung transplantation. With our innovation we hope to make an important contribution to the field of clinical medicine and to significantly improve patient outcomes in lung transplantation".

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##### Ischemia Reperfusion Injury

Restoration of blood supply to an organ after a critical period of ischemia results in parenchymal injury and dysfunction of the organ referred to as reperfusion injury. Ischemia reperfusion injury is often seen in organ

transplants, major organ resections and in shock. Despite refinements in lung preservation and improvements in surgical techniques and perioperative care, ischemia reperfusion-induced lung injury remains a significant cause of early morbidity and mortality after lung transplantation. The most common indications for lung transplantation are chronic obstructive pulmonary disease (COPD) including emphysema, idiopathic pulmonary fibrosis and cystic fibrosis. Ischemia reperfusion injury is the end result of multiple pathologic mechanisms. It is characterized by poor oxygenation as the main criterion for the condition and is also characterized by low pulmonary compliance, interstitial/alveolar oedema, pulmonary infiltrates on chest radiographs, increased pulmonary vascular resistance, intrapulmonary shunt and acute alveolar injury, as revealed by diffuse alveolar damage on pathology. Clinically, patients face prolonged ventilation, prolonged stays in intensive care in the hospital, increased medical costs, and increased risk of morbidity and mortality.

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#### About Orphan Drugs in the US

An orphan drug is a pharmaceutical agent that specifically treats a rare medical condition, the condition itself being referred to as an orphan disease. The US Orphan Drug Act is meant to encourage pharmaceutical companies to develop drugs for rare diseases. Under the law, companies that develop such a drug for a disorder affecting fewer than 200,000 people in the United States may sell it without competition for seven years and may get clinical trial tax incentives.

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## PRESS RELEASE

### **APEPTICO presents its inhalation therapy for prevention and treatment of Acute Lung Injury at the 2010 Annual Congress of the European Respiratory Society**

**15<sup>th</sup> September, 2010, Vienna, Austria: APEPTICO Forschung und Entwicklung GmbH, a biotechnology company developing a novel peptide-based drug for the treatment of the life threatening disease “Acute Lung Injury” today announced, that it will present its inhalation therapy for prevention and treatment of Acute Lung Injury at the Annual Congress of the European Respiratory Society which starts on 18<sup>th</sup> September 2010 in Barcelona, Spain.**

At the 2010 Annual Congress of the European Respiratory Society (ERS), APEPTICO will present its inhalation therapy for prevention and treatment of Acute Lung Injury to the scientific community. In his presentation, Dr. Bernhard Fischer, co-founder and CEO of APEPTICO, will summarise the design of bio-active peptides, the inhalation strategy of bio-active peptides into the respiratory tract and most recent results from the Acute Lung Injury ventilation study in the pig. Prof. Dr. Rudolf Lucas, co-founder and Chief Scientific Adviser of APEPTICO, will present the effects of the AP301 peptide on Listeriolysin-induced ENaC dysfunction in human airway epithelial cells. APEPTICO's bio-active peptides, such as AP301, have been designed to activate the epithelial sodium-ion channel (ENaC) of type II alveolar cells to facilitate alveolar liquid clearance during the life threatening condition Acute Lung Injury (ALI) / Acute Respiratory Distress Syndrome (ARDS). APEPTICO's lead compound AP301 has received Orphan Drug Designation both from the European Commission and from US Food and Drug Agency. Currently, AP301 is being assessed by APEPTICO for the treatment of lung injury and lung oedema caused by influenza and respiratory syncytial virus infections.

The ERS Congress is the largest international conference specialising in pulmonary medicine. It provides a unique forum where scientists and medical professionals from around the world have the opportunity to meet and exchange ideas and information in the field of respiratory medicine. The scientific programme of the ERS Congress aims to provide a perfect balance between clinical education and the latest scientific developments. The ERS Congress highlights key issues in the diagnosis, management and treatment of respiratory diseases, giving clinicians and research scientists the opportunity to report the latest findings in basic, clinical and population research.

Dr. Bernhard Fischer, CEO of APEPTICO commented: “I am pleased that the scientific organising committee of the ERS Annual Congress gives us the opportunity to present the progress of our drug development programme - the development of a new medicine for prevention and treatment of Acute Lung Injury / Acute Respiratory Distress Syndrome. Today no specific drug treatment exists for patients suffering from this life-threatening condition.”

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### About Acute Lung Injury (ALI)

Acute Lung Injury (ALI) is a pulmonary disorder characterised by acute onset, bilateral pulmonary infiltrates on chest radiograph consistent with pulmonary oedema, poor systemic oxygenation, and the absence of evidence of left arterial hypertension. There are many possible causes of ALI, such as inhaling high concentrations of smoke, toxins, or oxygen; severe burns; blood infections; lung infections; or trauma to other parts of the body. Acute Respiratory Distress Syndrome (ARDS) is the most catastrophic form of ALI.

Lungs contain alveoli, which are tiny air sacs where the oxygen is passed into the blood. In ALI blood and fluid begin to leak into the alveoli. When this happens, oxygen cannot enter the alveoli, which means oxygen no longer passes into the blood. Because the lungs are inflamed and filled with fluid, the patient finds it increasingly difficult to breathe. ALI is life-threatening because it makes breathing extremely difficult. The mortality rate of ALI/ARDS is 30% to 60% within 2 to 4 weeks.

Currently, no approved pharmacological therapy for ALI is available. ALI patients are treated with intensive support, which includes various strategies for assisted ventilation.

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