PRESS RELEASE

Apeptico and Mediolanum sign a Research & Development Cooperation and License Agreement for APEPTICO's therapeutic peptide Solnatide

Vienna, Austria and Milano, Italy, 2nd December 2016 - Apeptico Forschung und Entwicklung GmbH and Mediolanum farmaceutici S.p.A. today announce the signing of a Research & Development Cooperation and License Agreement for Apeptico's compound solnatide. Solnatide is a therapeutic peptide developed by Apeptico for the activation of alveolar liquid clearance, ready to enter into phase IIb clinical development for different life-threatening pulmonary indications.

Under the Agreement, Apeptico will receive an up-front research & development payment in cash, development milestones, and will supply Mediolanum the finished pharmaceutical product. In return, Mediolanum will receive an exclusive license for solnatide for various European markets.

Commenting on the agreement, Bernhard Fischer, CEO of Apeptico, stated: "We are very pleased that we could attract Mediolanum, a highly dynamic European pharmaceutical company, to license this exciting project. I am convinced that Apeptico's know-how in this area, together with the vision and the marketing capabilities of Mediolanum, are the best way forward to bring an innovative therapy to patients."

Commenting on the deal, Mr. Alessandro Del Bono, CEO of Mediolanum farmaceutici, said "2016 has been a very fruitful year for Mediolanum, particularly in regard to its efforts and achievements in R&D. We are delighted that we have been able to sign this agreement with Apeptico, a company at the forefront of innovation in the area of peptide-based treatments of pulmonary diseases. The addition of solnatide to our development pipeline is in line with our search for innovative solutions for the management of medical conditions with high-unmet medical need.

Mrs. Cristina Del Bono, Licensing & Business Development Director of Mediolanum added "We are proud to collaborate with Apeptico in their effort to bring to the market a new option for the treatment of patients affected with ARDS and PGD, two life-threatening conditions for which no satisfactory cure exists today. Beside in ARDS and PGD, Solnatide has received the orphan designation by the EMA also in high altitude pulmonary edema (HAPE) and pseudohypoaldosteronism type 1b, other two extremely severe conditions. Being the second deal that Mediolanum strikes in the orphan drug sector, it confirms and consolidates Mediolanum's will to be a strong player in this area, too."

About Apeptico Forschung und Entwicklung 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. Apeptico makes use of its technology platforms PEPBASE(TM) and PEPSCREEN(TM) to significantly reduce cost and shorten time to market of its drug candidates.

About solnatide

APEPTICO's proprietary therapeutic molecule solnatide (INN) is a synthetically manufactured structural equivalent to a domain of a human protein. Solnatide is being developed by Apeptico for the treatment of various forms of life-threatening pulmonary oedema. Liquid and dry powder formulations of solnatide can be directly administered into the lung by inhalation of aerosol particles with 5 micrometres diameter or less. Apeptico has successfully completed two phase IIa randomized controlled trials with orally inhaled solnatide, one for the treatment of patients with Acute Respiratory Distress Syndrome (ARDS) and one for the treatment of patients with primary graft dysfunction (PGD) following lung transplantation. Assessments for the treatment of high altitude pulmonary oedema (HAPE), pseudohypoaldosteronism type 1b (PHA type 1b) as well as severe cardiogenic pulmonary oedema are also underway.

About Mediolanum farmaceutici S.p.A.

Mediolanum farmaceutici SpA is a privately owned pharmaceutical company, headquartered in Milan. Founded by Mr. Rinaldo Del Bono in 1972, it has meanwhile grown to a 500 staff group and reached a consolidated turnover of around 200 million Euros. The Group also includes NeopharmedGentili Srl, a marketing company of pharmaceuticals in Italy, born from the merger of the two companies Neopharmed and Istituto Gentili, acquired from Merck Group; Cristalfarma Srl, a company that develops and commercializes food supplements from botanical sources in Italy; and the subsidiary Laboratoires Leurquin Mediolanum SA in France. In its 45 years' history, Mediolanum has submitted applications for more than 90 inventions, obtaining nearly 700 patents, and fully developed four new pharmaceutical products. Its current R&D pipeline comprises four projects. Beside the project with Apeptico on solnatide, Mediolanum's R&D pipeline includes GX-301, an immunotherapeutic vaccine in phase 2 for the treatment of prostate cancer; PP-001, a new small molecule entering clinical phase 1 for the treatment of uveitis, in collaboration with the Austrian company, Panoptes; and ACT-017, a humanized Fab in the preclinical phase of development for the treatment of acute ischemic stroke, in collaboration with the French company, Acticor. From a commercial point of view, Mediolanum's core business is focused on the vascular and cardio-metabolic area, including diabetes, the osteo-articular area and pneumology/allergology.

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PRESS RELEASE

APEPTICO announces break-through scientific results for the use of solnatide for the treatment of High Altitude Pulmonary Oedema

Vienna, Austria, 15th November 2016: APEPTICO, a privately held biotechnology company developing peptide drugs, today announced that in collaboration with Professor Zhou Qiquan from the Medical University in Chongqing it has produced breakthrough scientific results for the use of solnatide for the treatment of High Altitude Pulmonary Oedema (HAPE).

In a complex animal study, conducted in climate chambers simulating ascent to a mountain altitude of 6,000 meters, and continuation of exposure of test animals for several days to both hypobaric and hypoxic high altitude conditions, it has been demonstrated that solnatide reduced pulmonary oedema, increased occludin expression and improved gas-blood barrier function during acute hypobaric hypoxia and exercise in rats (HAPE model). The breakthrough results for the use of solnatide for the treatment of High Altitude Pulmonary Oedema (HAPE) were recently published in the scientific journal Chest (November 2016: http://journal.publications.chestnet.org/article.aspx?articleid=2583274).

In the HAPE model used, the results provide convincing evidence that the anti-oedema and anti-inflammatory properties of solnatide render it more effective than currently used drugs, aminophylline and dexamethasone. Furthermore, solnatide used to treat HAPE, may exert an inhibitory effect on p38-MAPK signalling pathways, as well as inhibiting NLRP3 inflammasome activation, stabilizing the NF–kappa B pathway and reducing the synthesis of cytokines and the inflammatory response. In addition, solnatide can increase expression of the tight junction protein occludin, thereby improving the stability of the alveolar capillary membrane, improving impermeability and reducing leakage of protein into the alveolar fluid.

These results provide a rationale for the clinical application of solnatide to patients exposed to high altitude hypoxia environment and developing symptoms of High Altitude Pulmonary Oedema.

Commenting on the scientific results, Bernhard Fischer, CEO of APEPTICO, stated: “We are very excited about the excellent study results obtained by our Chinese collaboration partner Professor Zhou Qiquan from the Medical University in Chongqing. They show that solnatide is not only effective in activating lung oedema clearance in patients at normal altitude, but also has a significant potential to become the first emergency and interventional travel medicine for tourist and trekkers climbing to high altitude areas in Europe, Asia, America and Africa.”

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About APEPTICO Forschung und Entwicklung 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. APEPTICO makes use of its technology platforms PEPBASE(TM) and PEPSCREEN(TM) to significantly reduce cost and to shorten time to market.

About solnatide

APEPTICO's proprietary therapeutic molecule solnatide (INN) is a synthetically manufactured structural equivalents to domains to a human proteins. solnatide is being developed by APEPTICO for the treatment of various forms of life-threatening pulmonary oedema. Liquid and dry powder formulations of solnatide can be administered into the lung by inhalation of aerosol particles with diameter 5 micrometres or less. solnatide activates the lung epithelial sodium channel (ENaC), located apically in alveolar epithelial cells, by directly binding to the crucial α-subunit of the channel, thus enhancing sodium ion uptake from the alveolar space across the alveolar cell membrane.

Solnatide has received orphan drug designation status for treatment of High Altitude Pulmonary Oedema by the European Commission and European Medicines Agency (EMA) and by the Food and Drug Agency (FDA).

About High Altitude Pulmonary Oedema

High altitude pulmonary oedema (HAPE) is a life-threatening complication of rapid ascents to altitudes higher than 3,000 m that usually occurs within the first 2–5 days after arrival at high altitude. At 6,000 meters, the standard barometric pressure is 47.2kPa (352 mmHg). At high altitude, the oxygen pressure falls below 50% of the sea level value. The reduced partial oxygen pressure in the atmosphere results in a drop of the alveolar and arterial oxygen pressure. During exercise and sleep, hypoxia is increased. Furthermore, temperature and atmospheric humidity decrease as well. In sum, climatic and environmental changes lead to exaggerated pulmonary hypertension leading to vascular leakage through over-perfusion, stress failure, or both. Individual susceptibility, rate of ascent, and pre-exposure to high altitude are major, independent determinants of High Altitude Pulmonary Oedema.

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PRESS RELEASE

APEPTICO's development compounds Solnatide has been granted Orphan Drug Designation for "Treatment of Primary Graft Dysfunction following Lung Transplantation" and "Treatment of Pseudohypoaldosteronism Type 1B" by the Food and Drug Administration

9th February 2016, Vienna, Austria: APEPTICO Forschung und Entwicklung GmbH, a biotechnology company developing novel peptide-based drugs, today announced that its development compound Solnatide has been granted Orphan Drug Designation for "Treatment of Primary Graft Dysfunction following Lung Transplantation" and for "Treatment of Pseudohypoaldosteronism Type 1B" by the Food and Drug Administration.

Pseudohypoaldosteronism type 1B (PHA 1B) is an autosomal recessive disorder caused by loss-of-function mutations in the epithelial sodium ion channel (ENaC). This life-threatening condition usually presents in the first weeks of life with severe dehydration, salt wasting and failure to thrive, symptoms which persist into adulthood. Patients often suffer from respiratory infections and may die from potassium overload and cardiac arrest. Currently, no satisfactory method of treatment exists.

Primary Graft Dysfunction (PGD) refers to acute allograft dysfunction within the first 72 h following lung transplantation in the absence of identifiable secondary causes. PGD is characterized by poor oxygenation and low pulmonary compliance; it affects approx. 30% of all lung transplant recipients for whom it represents a significant cause of early morbidity and mortality. Currently, no satisfactory method of treatment exists.

This was the first time that a development compound has been granted orphan drug designation for these life-threatening condition by the Food and Drug Administration. APEPTICO's request for orphan drug designation was based on results from experimental lung cell-based studies making use of heterologous expression of mutant versions of the human ENaC, and on data from APEPTICO's clinical study in lung transplant patients (PGD).

Prof. Bernhard Fischer, CEO of APEPTICO commented: "I am very pleased that the Food and Drug Administration has approved our applications for orphan drug designation for Solnatide for treatment of Pseudohypoaldosteronism type 1B and for treatment of Primary Graft Dysfunction following Lung Transplantation just few weeks after the positive decision of the European Medicines Agency. Until today there exist no approved therapies for these life-threatening conditions."

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Notes

About APEPTICO Forschung und Entwicklung 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 general risks associated with gene- and cell-technologies. APEPTICO makes use of its technology platforms PEPBASE(TM) and PEPSCREEN(TM) to significantly reduce cost and to shorten time to market.

About the APEPTICO's therapeutic protein structures

APEPTICO's proprietary therapeutic molecules, such as Solnatide (laboratory code AP301) are synthetically manufactured structural equivalents to domains of the human proteins. Liquid and dry powder formulations of such protein structures can be administered into the lung by inhalation of aerosol particles with diameter 5 micrometres or less. Most recently, APEPTICO has successfully completed two Phase II clinical trials with orally inhaled peptides for treatment of patients with pulmonary permeability oedema and ARDS (acute respiratory distress syndrome) and for treatment of patients with primary graft dysfunction following lung transplantation. For both acute and life-threatening conditions no specific drug-based treatments exist so far.

About Pseudohypoaldosteronism type 1B (PHA 1B)

Pseudohypoaldosteronism type 1B (PHA 1B) or autosomal recessive pseudohypoaldosteronism type I, is characterized by salt wasting from the kidney, colon, and sweat and salivary glands leading to high concentrations of sodium in sweat, stool, and saliva. The disorder involves multiple organ systems and is especially threatening in the neonatal period. Laboratory evaluation shows hyponatremia, hyperkalemia, and increased plasma renin activity with high serum aldosterone concentrations. Sweat and salivary glands, the distal renal tubule, and colonic mucosa are unresponsive to mineralocorticoids. In addition to severe dehydration, vomiting and failure to thrive occurring in the first weeks of life, the clinical picture may be complicated by cardiac dysrhythmias, collapse, shock or cardiac arrest. An increase in the volume of airway surface liquid leads to frequent respiratory tract manifestations and respiratory tract infections are common in affected children. PHA 1B is severe: no remission has been reported and patients suffer from recurrent life-threatening episodes of salt loss requiring salt supplements and control of hyperkalemia to ensure survival. PHA 1B is transmitted in an autosomal recessive manner and is caused by mutations in the genes coding for the subunits of the amiloride-sensitive sodium channel, ENaC resulting in the expression of mutant, loss-of-function ENaC.

About Primary Graft Dysfunction (PGD)

PGD after lung transplantation represents a multifactorial parenchymal injury and dysfunction to the transplanted lung that develops in the first 72 hours after transplantation in the absence of identifiable secondary causes.

The most common indications for lung transplantation are chronic obstructive pulmonary disease (COPD) including emphysema, idiopathic pulmonary fibrosis and cystic fibrosis. Other indications include alpha1-anti-trypsin deficiency emphysema, idiopathic pulmonary arterial hypertension, and sarcoidosis.

PGD is characterized by poor oxygenation and low pulmonary compliance as the main criterion for the condition, formation of interstitial & alveolar oedema, pulmonary infiltrates on chest radiographs, increased pulmonary vascular resistance, intrapulmonary shunt and acute alveolar injury, as revealed by diffuse alveolar damage (IDAD) on pathology. PGD occurs in approx. 30% of lung transplant recipients and it represents a significant cause of early morbidity and mortality to lung transplant patients.

About Orphan Drugs

An orphan drug is a pharmaceutical agent that specifically treats a rare medical condition, the condition itself being referred to as an orphan disease. Orphan drug legislation aim to encourage pharmaceutical companies to develop drugs for rare diseases. Under the law, companies that develop such a drug for an orphan disorder gain marketing exclusivity for 10 years (EU) and 7 years (USA) after marketing approval.

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