POTENTIATION OF ERYTHROPOIETIN ACTION BY MEMBRANE STEROID RECEPTOR AGONISTS

OFFERING HIGHLIGHTS

- Novel technology targeted at the potentiating the function of erythropoietin (EPO)
- Enhancers of the action of EPO can be used in conjunction with lower doses of EPO in the treatment, for example, of anemia in cancer patients
- Discovery addressing the FDA suggestion to physicians to use the lowest possible dose of EPO
- Specific steroid membrane receptor agonists are available for licensing
- The patented steroid membrane receptor agonists are currently in clinical development for cancer treatment
- Seeking worldwide licensee of novel use of novel steroid membrane receptor agonists as potentiators of EPO action

COMPANY PROFILE

Bionature EA, Ltd., headquartered in Nicosia, Cyprus, is a privately held biomedical research and pre-clinical development company established in 2003. Bionature seeks to discover new technologies that will enable the diagnosis, prevention, and treatment of diseases that contribute to chronic diseases and human aging. The Company focuses on the following main areas:

- Oncology, anti-tumor therapy
- Neuroprotective activities of natural and synthetic compounds
- Chronic inflammatory conditions
- Clinical diagnostics

Bionature seeks to achieve these goals by in-licensing discovery stage technology, building the intellectual property, performing pre-clinical development, and ultimately out-licensing the technology at the late pre-clinical / early clinical development stages. Bionature leverages its partnerships with academic centers to create synergy in applied and clinical research in the biomedical sciences, and in the development, testing and marketing of innovative pharmaceuticals and other biomedical products. Bionature currently has a strategic partnership with Emergo, an international private equity company, as well as a research partnership with the University of Crete Medical School. Bionature is actively looking for licensing partners.

TECHNOLOGY OVERVIEW

Bionature’s erythropoietin (EPO) invention relates to the use of membrane steroid receptor agonists as potentiators of the action of the best-selling erythropoiesis agent, EPO. More specifically, macromolecular conjugates of steroids with proteins of any kind (serum albumin, antibodies, or other proteins, which do not permit them to enter the cell and therefore designate them as agonists of the membrane receptors) or micromolecules, acting as agonists on these specific sites, are used as enhancers of the action of EPO in haemopoietic or extra-haemopoietic tissues. The invention claims that EPO and the membrane receptor agonists may be used conjointly in a kit, in order to decrease the administered doses of EPO and to minimize its side-effects, to control proliferation, differentiation, migration and regeneration of cells, in different organs and tissues. For example, EPO is commonly given to cancer patients to alleviate fatigue and to counter anemia, the most common cancer-associated morbidity. A growing body of evidence suggests that EPO may shorten survival in cancer patients and might possibly fuel tumor cell growth. In March 2007, the FDA added a black-box warning to EPO’s prescribing information that included a warning that EPO “may cause thrombogenic events… and increase the risk of death...” It warned physicians to “... use the lowest dose...”. Bionature’s discovery could help reduce the dosage of EPO required to have the desired anti-anemic effects and thus reduce the risks associated with the higher doses of EPO in cancer patients.

PARTNERSHIP / LICENSING OPPORTUNITIES

Bionature EA, Ltd. is currently seeking worldwide strategic partners to continue development of its EPO technology for the safer treatment of patients currently receiving EPO. The opportunity also exists for the licensing of specific membrane steroid receptor agonists that are being developed as anti-tumor agents. Bionature has several patent applications filed in the USA and in the EU.
BRIEF MARKET OVERVIEW

The total US sales for erythropoietins (EPO) in 2006 were $10 billion up from $6.4 billion in 2004. The recent attention to safety concerns notwithstanding, sales of EPO and the number of dispensed prescriptions were 4% higher in the first quarter of 2007. Johnson & Johnson, AMGEN and Hoffman La Roche, all have blockbuster EPO products on the market. An estimated 300,000 patients take EPO each year. Further to the approval by the FDA of new labeling for EPO products strengthening the Boxed Warning and Warnings sections of the labeling, there is a demand for agents that would help mitigate the risks associate with EPO administration to cancer patients.

MANAGEMENT TEAM

Achilleas Gravanis, PhD
Dr. Gravanis is Professor of Pharmacology at the University of Crete Medical School. His special research interests include modulation of the proliferation, apoptosis, and differentiation of neural and neuroendocrine normal and tumor cells. In addition, his interests lie in neurodegenerative diseases and neuroprotective agents. Dr. Gravanis has published more than 100 papers in MedLine journals.

Elias Castanas, MD, PhD, DSc
Dr. Castanas is currently a Professor of Experimental Endocrinology, at the University of Crete Medical School and Director of the Endocrinology Laboratory at the University Hospital of Heraklion in Crete. Special research interests: Modulation of the proliferation of hormone sensitive tumours by biologically active substances (opioid peptides and analogues, antioxidant polyphenols, and neuroactive steroids). Dr Castanas published more than 100 papers in peer-reviewed journals and several US and European patents.

Constantinos Neophytou, PhD
Dr. Neophytou is a portfolio manager with the private equity group, Emergo and is the Managing Director of Bionature. He holds a B.A. and an M.A. in Natural Sciences at Cambridge University and a Ph.D. in Neuroscience from University College London. He was a post-doctoral fellow at Harvard Medical School as a Welcome Trust Prize Scholar. Prior to joining Emergo, he worked for three years as the General Manager of a financial services group and the venture capital firm BOC Ventures in Cyprus. He is on the BOD of a number of emerging Companies, in the biomedical sector and in the information and communication technology sectors. Dr Neophytou has close to 10 years experience in private equity transactions in the biomedical sector.

• EPO market at $10 billion in the USA (2006) and rising
• Data from recent clinical studies with patients who received EPO prompted the FDA to approve new labeling for the use of EPO products in patients with cancer
• Bionature’s product could help reduce the dose of EPO required in cancer patients to have the desired effects
• Accomplished scientists in the fields of chemistry, endocrinology, and pharmacology
• Bionature’s scientists published more than 250 peer-reviewed scientific papers