Oxis Biotech Files U.S. Patent Application Covering p62/Sequestosome 1 Inhibitors For The Treatment Of Multiple Myeloma And Secondary Osteolytic Lesions

TAMPA, Fla., June 4, 2015 -- Oxis Biotech, Inc. (OXIS), a wholly owned subsidiary of Oxis International, Inc. [OTC: OXIS] announced today it has filed a U.S. patent application covering additional analogs of the company's lead compound, OXS-4235, a potent p62/Sequestosome 1 (p62) inhibitor. These novel p62 inhibitors demonstrate inhibition of multiple myeloma cell growth without toxicity to normal bone marrow stromal cells. Bone marrow stromal cells are involved in hematopoiesis and certain inflammatory processes.

Multiple myeloma is a type of cancer that forms in white blood cells, and affects about 26,850 people annually in the USA causing about 11,240 deaths per year. Multiple myeloma causes cancer cells to accumulate in the bone marrow, where they crowd out healthy blood cells. Multiple myeloma is also characterized by destructive osteolytic bone lesions (rounded, punched-out areas of bone), diffuse osteoporosis, bone pain, and the production of abnormal proteins which accumulate in the urine. Plasma cell leukemia, a condition in which plasma cells comprise greater than 20% of peripheral leukocytes, is typically a terminal stage of multiple myeloma and is associated with short survival.

Multiple myeloma is marked by abnormal protein production, and frequently is characterized by bone disease – a major cause of patient morbidity. Multiple myeloma induced bone disease is marked by holes in the bone and intense pain due to increased osteoclast bone degradation activity and highly suppressed or absent osteoblast bone remodeling (growth) activity. Cell adhesive interactions between multiple myeloma cells and bone marrow stromal cells activate multiple signaling pathways that enhance cancerous tumor growth and bone destruction while suppressing new bone formation and contributing to drug resistance.

The recent improvements in overall survival and remission duration in multiple myeloma are largely due to the advent of novel therapeutic agents. These therapeutic agents exploit a tumor cell's dependency on clearance mechanisms for abnormal or mutant cellular proteins. Tumor cells are very sensitive to any type of inhibition of this clearance mechanism which when inhibited leads to an antiproliferative and pro-apoptotic effect on the tumor cells mediated by induction of endoplasmic reticulum stress, activation of caspases, and generation of reactive oxygen species.

p62 is a protein having multiple biological roles involving cell signaling, cell receptor internalization, and protein degradation/turnover. p62 has been reported to be a regulator of inflammation, neurogenesis, increased osteoclastogenesis (bone destruction), adipogenesis and T-cell differentiation. One of the more interesting functions of p62 is the regulation of NF-kappa-B, which is the master regulator of innate immunity and aging. p62 is also found in inclusion bodies containing polyubiquitinated protein aggregates which are present in several neurodegenerative diseases such as Parkinson, Alzheimer, and Huntington's diseases. Additionally, p62 acts as s shuttling factor for the delivery of damaged biomolecules to the proteasome for destruction and removal.

By selectively inhibiting p62 in multiple myeloma cancer cells, stress is induced in the multiple myeloma cancer cells due to the accumulation within the cells of damaged biomolecules that cannot be destroyed via the normal function of the proteasome. As a result of the stress placed on the cancer cells by inhibition of p62, the cancer cells undergo a biological process known as autophagy which results in their destruction.

OXS-4235 is a first-in-class therapeutic candidate targeting the inhibition of p62 for the treatment of multiple myeloma and osteolytic lesions. In *in vitro* and *in vivo* models of multiple myeloma and osteoporosis, OXS-4235 demonstrated the ability to kill multiple myeloma tumors, decrease osteolytic lesions, and the ability to help restore normal bone remodeling resulting in healthy bone. In addition to

direct killing of multiple myeloma cells, OXS-4235 was found to also inhibit TNF-alpha mediated osteoclast formation. TNF-alpha is a major suppressor of osteoblast differentiation. TNF-alpha is upregulated in the bone marrow microenvironment resulting from multiple myeloma cell – stromal cell interactions. Reducing osteoblast suppression in the multiple myeloma bone marrow microenvironment via the inhibition of TNF-alpha, normal bone remodeling is restored.

"OXS-4235's dual mechanism of action, and no observed toxicity in mouse models of multiple myeloma is very exciting". Our drugs ability to increase bone density while shrinking tumors, which is a major problem with Multiple Myeloma patients, Makes this a first of its kind, as there are no other drugs with this dual mechanism of action (approved or not approved) that have this ability, stated Anthony Cataldo, Chairman and Chief Executive Officer of Oxis Biotech, Inc.

About Oxis Biotech, Inc.

Oxis Biotech is a cancer immunotherapy company developing innovative therapies focused on the treatment of cancer. Oxis' immunotherapy platform includes bispecific immune cell engagers, antibody-drug conjugates (ADCs), and novel small molecule therapeutics targeting B-cell malignancies and certain solid tumors such as triple negative breast cancer.

Forward-Looking Statements

Except for historical information contained herein, the statements in this release are forward-looking and made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are inherently unreliable and actual results may differ materially. Examples of forward-looking statements in this news release include statements regarding the payment of dividends, marketing and distribution plans, development activities and anticipated operating results. Factors which could cause actual results to differ materially from these forward-looking statements include such factors as the Company's ability to accomplish its business initiatives, significant fluctuations in marketing expenses and ability to achieve and expand significant levels of revenues, or recognize net income, from the sale of its products and services, as well as the introduction of competing products, or management's ability to attract and maintain qualified personnel necessary for the development and commercialization of its planned products, and other information that may be detailed from time to time in the Company's filings with the United States Securities and Exchange Commission. The Company undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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