



## **A novel class of mTOR inhibitors (Zheng, RWJ 06-34) *Oncology***

### **Background**

Mammalian target of rapamycin (mTOR) is an important drug target for many human diseases, including graft rejection, autoimmunity, restenosis, cancer, heart disease, diabetes, obesity, aging, and also Alzheimer, Parkinson and Huntington diseases. mTOR is a conserved regulator of cell growth and metabolism that integrates energy, growth factor, and nutrient signals. TOR is a phosphatidylinositide 3-kinase-related kinase (PIKK). It forms two multiprotein complexes mTORC1 and mTORC2. Only mTORC1 is sensitive to rapamycin. mTOR localizes to the endoplasmic reticulum (ER) and Golgi. Dysregulation of mTOR signaling occurs in diverse human tumors. Preclinical studies indicate that rapamycins are potent inhibitors of the proliferation of numerous tumor cell lines in culture and of murine syngeneic tumor models or human Xenografts.

### **Description of Technology**

A novel class of mTOR inhibitors targeting both mTORC1 and mTORC2 were identified. The inhibitors are more potent than and distinct from rapamycin and rapamycin-derivatives in their mechanism of action. They block localization of mTOR to the ER and Golgi. They also induce apoptosis in tumor cells a distinctive advantage for cancer therapy. Moreover, because mTORC2, an important regulatory kinase in the aging pathway is inhibited, they can be useful agents to treat aging and aging-related illness.

### **Applications**

- These new inhibitors can be used to develop drugs with clinical utility in the treatment of many human diseases involving mTOR dysregulation.
- This technology can also be used for drug discovery targeting ER and Golgi localization of mTOR.
- The technology can also be applied in the research area to target molecules to the ER and Golgi.

### **Patent Status**

United States Provisional Application for Patent was filed on December 8, 2006

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