New chemical family
of dual PI3K and mTOR inhibitors

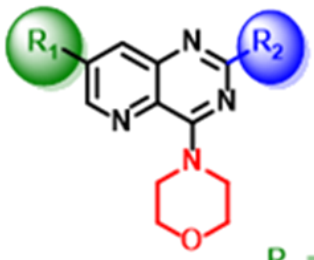
HEALTH
ONCOLOGY

PROMISING DRUGS TO TREAT CANCER

The phosphatidylinositol-3-kinase (PI3K)/Akt and the mammalian target of rapamycin (mTOR) signaling pathways are both crucial to many aspects of cell growth and survival, in physiological as well as in pathological conditions. The PI3K/Akt pathway is a key regulator of survival during cellular stress. Since tumors exist in an intrinsically stressful environment, the role of this pathway in cancer appears to be crucial.

The available compounds target the PI3K, Akt and mTOR pathway, largely involved in several cancers progreesion.
The selected molecules have beneficial properties compared to other products under development.

Inhibitors of the PI3K/AKT/mTOR pathway are mostly tested for advanced or metastatic tumors in combination with other chemotherapeutic treatments, and often as second-line therapy when a first treatment has failed or when the tumors cannot be removed by surgery.



R_1 = Alkyl, Aryl.
R_2 = Aryl.

Competitive Advantages

- Synthesis and screening of new dual PI3K/mTOR inhibitors have been used to create a portfolio of 100 active small molecules with 3 leads tested for oncology;
- Novel and IP protected family of compounds: compounds have both PI3K and mTOR targets. This combined activity should lead to a strongest inhibition of the whole PI3K/Akt/mTOR pathway,
- Nanomolar range of enzymatic and cellular activities exhibiting specifity on both targets (PI3K and mTOR) with an acceptable kinase selectivity profile,
- A wide spectrum of indication,
- Low toxicity and good stability relative to compounds under clinical development,
- Proven *in vivo* efficacy versus molecule under clinical development.

Development Status

- Thorough structural study when designing pharmacophores
- Optimized synthesis for selected derivatives
- Preclinical evaluations includeScreening against PI3K-mTOR for specificity
  - Screening against several cell lines for selectivity
  - *In vitro* mechanistic studies on the cell cycle
  - *In vitro* determination of PK / PD, solubilities, plasma and liver microsomal stabilities and clearance parameters.
  - *In vivo* PK / PD parameters, acute and repeated dose toxicities
  - *In vivo* efficacy using orthotopic model of colon cancer

Business Opportunities

- Opportunity to address multiple markets from inflammation to rare diseases
- Adjuvant therapy with appouved therapeutics
- Large, underserved in rare diseases
- Human and veterinary markets
- Possibility of Orphan Drug Designation on specific indications

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#Keywords

PI3K/mTOR Pathway
Inhibitors
Chemotherapy
Small molecules

Research Team

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Partnership

Licensing or co-development

Intellectual Property

FR2994572
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