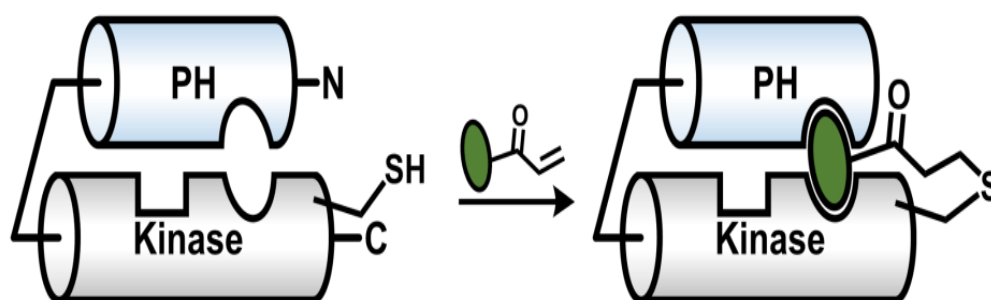


CAAI - Covalent-allosteric AKT inhibitors

Inhibitors of the AKT pathway with a new mode of binding

Invention

The development of new drugs in oncology has shifted from unspecific cytotoxic drugs to highly specific substances with known targets and modes of action. A prominent group of these target specific cancer drugs are the kinase inhibitors. The invented substances are inhibitors of the kinase AKT which is involved in several pathways regulating cell functions in cancer, e.g. survival and proliferation. The particular novelty of the invented compounds is based on their combined covalent-allosteric binding mode. These are first-in-class modulators of AKT with a novel mode of inhibition. Covalent-allosteric inhibitors show extended drug-target residence times.



Covalent-allosteric inhibitors (green) binding to the interface of the pleckstrin homology (PH) and the kinase domain, thereby keeping AKT in its enzymatically inactive conformation (taken from Weisner et al., DOI: 10.1002/anie.201502142R1).

Commercial Opportunities

AKT is a serine/threonine kinase and oncogene that has already been identified and addressed as a target in cancer therapy by several pharma companies. The invented substances are of high interest for any pharma company with an oncology pipeline and are of special advantage for those who seek to improve, broaden or supplement their kinase inhibitor portfolio.

Current Status

Binding specificity as well as an IC_{50} of 0.2 nM for the most promising compound have been determined by *in vitro* experiments so far.

On behalf of the Technical University (TU) of Dortmund, PROvendis offers access to rights for commercial use as well as the opportunity for further co-development. In case of interest we will be pleased to inform you about the patent status.

Relevant Publications

- Weisner, J., *et al.* (2015) Covalent-allosteric kinase inhibitors. *Angewandte Chemie* 54(35): 10313-6
- Vivanco, I., *et al.* (2014) A kinase-independent function of AKT promotes cancer cell survival. *eLife* 31: 3.
- Barf, T. & Kaptein, A. (2012) Irreversible protein kinase inhibitors: balancing the benefits and risks. *J. Med. Chem.* 55: 6243-62.
- Hers, I., *et al.* (2011) Akt signaling in health and disease. *Cell. Signal.* 23: 1515-27.
- Garcia-Echeverria, C. & Sellers, W.R. (2008) Drug discovery approaches targeting the PI3K/Akt pathway in cancer. *Oncogene* 27: 5511-26.

An invention of the Technical University of Dortmund.

Competitive Advantages

- AKT inhibitors with a new mode of action
- The inhibitors bind AKT irreversibly and specifically with highest affinity

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