

**P009** PI3K inhibitors in 2006 – 15 years of discovery after LY-294002

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The abstract discusses the current development status of PI3K inhibitors. In 1991 LY294002 was disclosed as non-selective PI3K inhibitor. But it was only ten years later that the first patents of new generations of PI3K inhibitors started to appear. Since then, many pharmaceutical companies and academic research labs have invested extensive efforts into developing isoform selective inhibitors. Today, over twenty different chemotypes of PI3K inhibitors are in the public domain, some of which show trends to isoform selectivity. The various chemotypes will be discussed and attempts to clustering will be made.

In a second part, PI3Kgamma inhibitors are examined in more detail. Inspection of the different chemotypes disclosed to date reveals an unusually high structural similarity between the compound series identified by different companies. Since the publications dates of the corresponding patent applications are very close to each other, it does not appear to be a fast-follower (“Me-Too”) effect, but rather a phenomenon of “convergent evolution”. This is illustrated in two independent cases. In a third part, as part of our research, this communication discloses a case study of an iterative improvement of PI3Kgamma inhibitors as potential RA drugs.