

Pyrimidine derivatives - Effective broad-spectrum antipicornaviral active ingredients

The innovation

Given the outbreak of diseases like AIDS, avian flu and swine flu, the causative agents of such infections, i.e. viruses, have gained increasing public awareness and interest. An eminently virulent class of viruses is embodied by rhino- and enteroviruses (family: picornaviridae), which comprise many important human (and animal) pathogens. Rhinoviruses, for instance, represent the most prominent (30-50%) causative agent of common cold and the most common virus in humans. Other diseases caused by rhino- and enteroviruses range from myocarditis, to meningitis and encephalitis, to poliomyelitis, and predominantly affect newborns and young children, as well as the elderly and people with compromised immune system.

Most of the picornaviral infections cannot be treated directly and there are currently no medications that have conclusively demonstrated to shorten the duration of illnesses. Development of a promising drug candidate (pleconaril) e.g. was discontinued or limited towards selected niche applications, due to major safety concerns and limited efficacy. The different diseases and lack of suitable treatment options are mainly due the rhino- and enteroviruses' tremendous variability. Indeed, more than 100 different serotypes of rhinoviruses

alone are known, and up to now no drug candidate could convincingly demonstrate that it would be capable of inhibiting replication of at least a significant proportion of picornaviruses.

Recent progress in the synthesis of antiviral compounds has yielded a new class of pyrazolo-pyrimidine derivatives that possesses broad-spectrum activity against most (if not all) rhino- and enteroviruses. One derivative, termed OBR-5-340, has been selected for further development, given its demonstrated low *in vitro* and *in vivo* toxicity, as well as excellent metabolic stability and bioavailability. Comprehensive pharmacological and toxicological studies revealed that the orally available API is well-tolerated in rats and mice even at elevated doses as well as after long-term exposure (1-month). First experiments in a Coxsackie B3 virus (CVB3)-induced myocarditis mouse-model also provided strong evidence about the API's *in vivo* efficacy. OBR-5-340 will be first developed against common cold and is anticipated to enter preclinical development in Q3/2010 and clinical phase I in Q1/2011. Development of OBR-5-340 or other pyrimidine derivatives, possessing a suitable spectrum of activity, against other picornaviral diseases is both feasible and intended.



Advantages at a glance

- Innovative pyrimidine derivatives for the treatment of entero- and rhinoviral infections (e.g. the common cold, myocarditis, meningitis)
- Broad spectrum of activity also against currently resistant viruses
- Extensive *in vivo* studies confirmed the API's good tolerance, high metabolic stability and efficacy
- Current stage of development: (active ingredient development phase completed) start of the preclinical development

To acquire a licence for this new technology, please don't hesitate to contact us!

Keywords

- Antiviral drugs
- Antiinfectives
- Rhinovirus
- Enterovirus
- Picornaviridae

Areas of application

- Treatment of entero- and rhinoviral infections (e.g. the common cold, myocarditis, meningitis)

Patent status

The invention is covered by a patent family that has been internationally filed and is owned by Dritte Patentportfolio Beteiligungsgesellschaft mbH & Co. KG. The first application was filed in June 2006.



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