

# Current Patents Gazette

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## DOLPHIN



The records appearing in this Gazette will be added to DOLPHIN, the database Of all pharmaceutical inventions in the next week. Based on the INPADOC database produced by the European Patent Office, it covers all national and international patents with relevance to pharmaceutical research and development published from 1968 onwards and selected patents from earlier years. DOLPHIN contains information on bibliographic data, contents, associated products, legal status, licensees and context of patents, which is presented in a format to convey all aspects of a patent at a glance.

## News & Highlights from Week 0737

Business news in the UK national press recently included positive product development indications for **AstraZeneca**, in relation to the anti-inflammatory drug it is developing in collaboration with **Pozen Inc**. The product, which is about to enter phase III trials, is a fixed-dose combination of AZ's **esomeprazole** with **naproxen**, suitable for long-term use by chronic pain sufferers, especially arthritis patients. Code-named **PN-400**, the combination uses Pozen's proprietary formulation technology. Surprisingly perhaps, it is eleven years since **Astra AB** initiated the patent application in which the combination is first claimed, **WO9725064**. This now has granted family members in both Europe and the US, where normal patent expiry dates will fall at the end of 2016, and on this basis the product would be expected to enjoy no more than about seven year's patent protection once it is approved for marketing. However, the patent protection is already complicated by the existence of several divisional applications and continuations, and in addition there will be the possibility of term extensions and Supplementary Protection Certificates (SPCs) once marketing authorization is obtained. In view of these complications, it is hardly surprising that AZ is already quoting a US patent expiry date of 2023 for the product, and this may well be based on claims in Pozen's **WO02098352**. However, the full scope of protection for PN-400 may not finally become clear until an Orange Book listing appears, following FDA approval.

The UK Patents and Designs Journal (PDJ) No. 6173 this week reports the expiry on August 22, 2007 of **Cancer Research Technology's** (CRT's) SPC for **temozolomide** based on **GB2104522**. SPCs on equivalents in other European countries mostly expired around the same date as did an extension granted in Australia. However, equivalent **US5260291**, which is listed in the Orange Book for CRT's

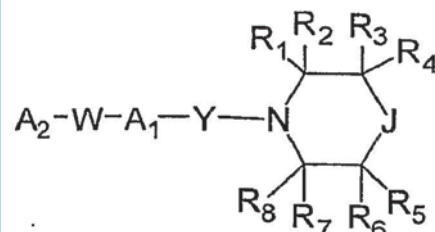
**Temodar** (temozolomide), will not expire until February 2014 as the term is based on 17 years from publication and it has also been granted a 1006 day extension plus 6 months additional pediatric exclusivity. In March 2007, **Barr Labs** filed an ANDA containing a paragraph IV certification for a generic Temodar product, which was accepted by the FDA in June. **Schering Corp** and CRT filed suit in the US District Court for Delaware in July to prevent Barr from proceeding with the commercialization of its product. This action formally initiates the patent challenge process under the Hatch-Waxman Act. Worldwide sales of temozolomide reported by **Schering-Plough** for 2006 were \$703 million, representing a 20% year-on-year growth and in April 2007, Atlantic Equities analysts said that Temodar had become one of the drugs of choice for malignant brain tumors, and they expected it to remain at the core of all treatments.

In Japan, the August Gazette published details of four extension applications by **GD Searle (Pfizer)** for **celecoxib (Celebrex)**, two by **Kirin-Amgen** for **darbepoetin alfa (Aranesp)** and three by **Kyorin Pharma** for **imidafenacin**. No new granted extensions were reported.

**York Pharma** has filed an initial UK application for improved skin barrier function. This seems to read directly on to the skin protease inhibitor development program that the company is now once again pursuing under the code **YP-001**. Prior to the company's February 2005 acquisition of **Molecular SkinCare**, this Skin Barrier Repair (SBR) technology was known as **MP-001**, and the trade name **Sabarep** is also associated with it. The handful of earlier patent applications from York Pharma includes **WO2007020479** with claims to topical compositions containing microparticulate zinc compounds. A second SBR product now appears in the company's product listing, coded **YP-002**, and the April 2007 acquisition

of **Rosanto Pharmaceuticals** gave access to a topical anti-TNF $\alpha$  psoriasis treatment.

**Lectus Therapeutics** this week filed five UK initial applications all entitled "Calcium ion modulators and uses thereof". A **University of Bristol** spin-out company, Lectus focuses on the discovery and development of ion channel therapeutics for urinary bladder disorders, pain and angina. In September 2007, Lectus secured £3million in investment capital from the **Wellcome Trust** to fund a specific program to identify new classes of potassium channel modulator drug candidates for the treatment of multiple sclerosis. Lectus' investors include **Takeda Research Investment** (the corporate venture arm of Takeda), **Astellas Venture Management** (the venture capital arm of Astellas), and two top-tier European venture capital companies, **Sofinnova Partners** and **Quester**. The company has recently developed a novel cell-free assay technology, LEPTICS (Leveraged Enabling Proteomics Technology for Ion Channel Screening) for the identification and development of "second-generation drugs" that selectively targets ion channels.



First patenting to emerge from Trimeris on gp120/CD4 interaction inhibitors for the treatment of HIV and AIDS

## UK initial ("A0") applications filed July 30th – August 5th 2007

**Asterion** has filed a series of four UK initial applications relating respectively to **erythropoietin** (GB0715126), **granulocyte colony stimulating factor** (GB0715133), **leptin** (GB0715216), and **IGF-1** (GB0715213). Asterion specializes in the development of **cytokine receptor agonists and antagonists** and was formed in 2001 as a collaboration between the University of Sheffield Medical School and the department of Molecular Biology and Biotechnology. In February 2006 Thomson analysts reported an application filed in January regarding a leptin ligand that probably followed on from WO2005003165, which covers a range of cytokine variant polypeptides. We can now see the resultant publication, WO2007080404, claiming preparation of leptin antibodies. This week's leptin related application seems to represent a continuation of this work. The variant polypeptides covered in WO2005003165 encompass most of this week's UK initial application topics, and in May 2006 we reported another similar broad initial application, entitled simply "**Polypeptide antagonists**"; if it is proceeding, this case should be **published in early October 2007**. The increasingly specific nature the company's applications could well reflect more explicit areas of endeavor or possibly just a change in application style; this is the first time we have seen an application or publication by Asterion directed exclusively at IGF-1. It is interesting to note **Asterion's adoption of more specific titles for its patent applications**, which could correspond to a clearer focus on products suitable for commercialization.

**Glaxo Group** is seeking patent protection (GB0714815) for **pyrazolo[3,4-b]pyridine compounds** and their use as **PDE4 inhibitors**. This unusually explicit title might seem at first sight to be giving away more information than is strictly necessary at this stage. However, the company has at least half-a-dozen published PCT applications disclosing the use of this **bicyclic template** for potential PDE4 antiinflammatories, beginning with WO2004024728. Despite this intensive discovery activity over a five-year period, no clear lead candidate seems to have emerged from this program to date.

**Inion** has filed two UK initial applications (GB0714975 and GB0714791) for "**catecholamine metabolism modulators**" and "**osteogenic compounds**". The first of these applications appears to be a departure from Inion's usual activities. Inion is a Finnish company, specializing in the **development of biodegradable medical implants** such as plates, pins, screws and membranes, for treatment of skeletal injuries. The company website lists proprietary Inion Optima™ polymeric materials which can be tailored to degrade at a certain rate, so as to gradually transfer load to bone to stimulate regeneration. Current research is focused on incorporation of bone growth factors (probably related to the "osteogenic compounds") into these implants. It is likely that the catecholamine metabolism modulators will be formulated in the same way.

**NV reMYND** has filed a sequence of seven UK initial patent applications claiming a variety of **heterocyclic compounds** for use in treating **neurodegenerative diseases**. Unusually, the actual template used is specified in the title of each application, as follows: **thiadiazolyl piperazines** (GB0715227 and GB0715255), **thiadiazoles with heterocyclyl and aliphatic sulfonamidopiperazinyl substituents** (GB0715192 and GB0715260), **benzyl and phenyl thiazolylpiperazines** (GB0715256 and GB0715257), and **aromatic derivatives** (GB0715253). All seven applications were filed in the first week of August 2007, just days before publication of WO2007090617, only the Belgian company's third published PCT application, and the only one so far relating to potential therapeutics. The two previous applications relate to drug discovery models, describing the use of transgenic yeast cells in the study of tau-opathy and amyloidogenic protein toxicity; both have input from KU Leuven, from which reMYND was spun off in 2002. It is virtually certain that the seven new applications build on the series of thiadiazoles claimed in the recent '617 publication. This in turn is probably the program that the company refers to as **ReS9-S**, which is reported to have yielded a large family of analogous compounds exerting a cytoprotective effect on neuronal cell cultures. The expectation is that one or more candidates from this series will enter clinical trails for Parkinson's disease during 2008.

**The Medical Research Council** has this week filed a UK initial application entitled '**Crystal structure of AMPK and uses thereof**'. The only record related to this that we have is WO2004113562, co-assigned to Columbia University, disclosing the use of AMP-activated protein kinase in assaying LKB1 serine threonine kinase activity. The application later goes on to claim the use of **AMPK in treating Peutz-Jeghers syndrome, obesity, diabetes and hypercardiomyotrophy**. This filing may discuss or be related to previous literature articles (e.g. Biochemical and biophysical Research Communications 337 (2005) 1224-1228) which discuss the crystal structure, at 2.2 angstrom resolution, of the protein kinase domain (KD) of the catalytic subunit of yeast AMPK (SNF1). However this is more so for understanding the molecular basis for AMPK function.