

Current Patents Gazette

ISSUE 0744 2nd November 2007

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 0744

The UK Patent and Designs Journal (PDJ No. 6180) this week gives details of three Supplementary Protection Certificate (SPC) applications filed and one SPC expiration. Two of the applications were reported in the Current Patents Gazette 0742 two weeks ago and are applications by **Pfizer Health AB** and **Schwarz Pharma AG** covering **fesoterodine (Toviaz)**. Approved for the treatment of overactive bladder (OAB) in Europe Toviaz has also received an approvable letter from the FDA in the USA. If the SPCs on **EP1077912** and **EP1019358** are granted, protection on both patents will be extended to April 2022, fifteen years after the earliest EU Marketing authorisation.

The remaining SPC application was filed by **Mallinckrodt** on **EP0425571** and covers its imaging agent **gadoversetamide (Optimark)**, an injectable magnetic resonance imaging (MRI) agent designed for increased enhancement of lesions of the brain, spine and liver, including, but not exclusive to, tumors. US approval took place much earlier and the product was launched in the US in March 2000. If granted, the SPC will expire July 18 2014, five years after entering into force.

Alongside the filed applications, the PDJ gave notice that the SPC based on **EP077754** covering **quinagolide** had expired October 5, 2007. **Quinagolide** was launched by **Sandoz** as **Norprolac** for the treatment of hyperprolactinemia. In 2004, **Ferring Pharmaceuticals** obtained the worldwide manufacturing, marketing and distribution rights of quinagolide from **Novartis** and was also developing the drug for the potential prevention of ovarian hyperstimulation syndrome.

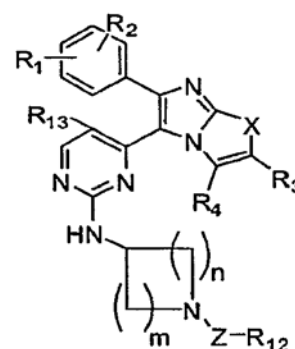
In August, the **US Patent and Trademark Office (USPTO)** published a final rule notice in

the Federal Register (Fed. Reg. 46716 Aug. 21, 2007) revising the rules of practice in patent cases relating to continuing applications and requests for continued examination practices, and for the examination of claims in patent applications. This notice indicated that the effective date for the changes to the rules of practice in the Claims and Continuations Final Rule was to be November 1, 2007. However, on October 31, 2007, the US District Court for the Eastern District of Virginia, issued a Preliminary Injunction enjoining the USPTO from implementing the changes in the Claims and Continuations Final Rule. Therefore, the changes to the rules of practice in this Rule did not go into effect on November 1, 2007. The USPTO notice states that it will continue processing and examining patent applications under the rules and procedures in effect on October 31, 2007, until further notice.

In Japan, the October Japanese Patent Gazette reports that **Roche** has been granted patent extensions for two of its drug products. More than one year has been added to the life of **JP3090305**, for the use of **valganciclovir** for the treatment of cytomegalovirus (CMV) retinitis in patients with AIDS. Valganciclovir is marketed in Japan as **Valixa** and as **Valcyte** or **Cymevene** in other parts of the world and achieved sales of almost around \$390 million in 2006. The patent now expires in September 2016 in Japan, which matches the expiry dates in Europe, where granted SPCs will expire approximately one week earlier. **Mitsubishi Tanabe** currently holds the Japanese marketing rights. Roche has also been granted almost 6 months extension on its **JP3839667** for its **Copegus** tablets, used in treating chronic Hepatitis C (HCV) infection. Copegus is a combination of **ribavirin** with Roche's **Pegasys (pegylated interferon alfa-2a)**. Ribavirin has been licensed to Roche for use in the combination by **Schering-Plough** and **ICN**

Pharmaceuticals. Sales of ribavirin alone have been declining at around \$310 million in 2006. However, sales of Pegasys and Copegus are on the increase reaching over \$1.1 billion in 2006. This extension will protect the combination in Japan until November 2019.

BMS' Baraclude (entecavir), a viral replication inhibitor and cyclopentyl guanosine analog used for the once-daily oral treatment of chronic HBV infection, was granted an extra five years protection based on **JP3068858**, which will now expire October 2016. Although launched in the US in April 2005, European and Japanese launches did not take place until Q3 2006 and so 2006 sales were only around \$83 million (around 12% of the HBV franchise). However sales are predicted by our Thomson-Pharma analysts to grow rapidly to about \$500 million by 2010, which is estimated to be over a third of the franchise and would see Baraclude vying with **GSK's lamivudine** for leadership of the HBV franchise.



First patenting to emerge from ArQule on their B-Raf kinase inhibitor program

UK initial ("A0") applications filed September 17th – September 23rd 2007

Istituto di Ricerche di Biologia Molecolare P Angeletti (IRBM) has filed a new UK initial application claiming **nucleoside derivatives as inhibitors of viral polymerases** on September 24 2007 (GB0718575). Possibly linked to nucleoside aryl phosphoramidates recently claimed by Angeletti as precursors to inhibitors of RNA-dependent RNA viral polymerase in **WO2007095269**, useful for the treatment of hepatitis C viral infection. Merck is currently developing MK-0608, a nucleoside inhibitor of NS5B hepatitis C virus (HCV) RNA-dependent RNA polymerase, for potential in HCV, which by December 2006 had entered phase I trials.

K U Leuven R&D filed two new UK initial applications covering modified nucleotides on September 17 2007, describing their **use as a substrate for polymerases and antiviral agents**. (GB0718228 and GB0718229). Leuven's Rega Institute, has previously developed adefovir dipivoxil (licensed to and launched by Gilead) an HIV-1 reverse transcriptase and DNA polymerase inhibitor targeted at Hepatitis B, HIV, pox and cytomegalovirus infection. Rega is also investigating a series of reverse transcriptase inhibitors, including TSAO-T. Specifically, TSAO-T has been described as a highly specific non-competitive inhibitor of the RNA-dependent DNA polymerase function of HIV-1 RT.

NPIL Pharmaceuticals (UK) is seeking to protect a process for **preparing sulfonamides** (GB0718359). The applicant appears to be the UK arm of Nicholas Piramal India Limited, which at the beginning of 2003 merged with Global Bulk Drugs & Fine Chemicals Pvt. On the face of it, nothing in the past patenting of either company seems directly relevant to the present application. However, NPIL has been working on *p*-nitrobenzenesulfonamides in the context of HIV protease inhibitors such as amprenavir, as set out in **WO2006131757**. The new application may represent a further improvement in that manufacturing process, and its filing in the UK may signify a link with NPIL's recent purchase of the former Pfizer manufacturing facility at Morpeth in Northumberland.

Protherics Medicines Development and **Advanced In Vitro Cell Technologies (AdvanCell)** have jointly filed a UK initial patent application (GB0718239), covering **novel therapeutic use of an aminoimidazole derivative**. The significance of this application would not be apparent, were it not for the University of Barcelona's **WO03080076**, relating to acadesine. This is a riboside of 5-aminoimidazole-4-carboxamide, and the corresponding European patent granted in May 2006 has been transferred into the name of AdvanCell, whose website reports a development project on the use of acadesine in B-cell chronic lymphocytic leukemia, apparently in conjunction with ciclosporin. A 15 January 2007 press release reports the participation in this development project of Protherics, whose own portfolio includes **WO2006023388** with claims to ciclosporin formulations. Acadesine itself has been under investigation since the mid-1950s, though SICOR Inc seems to be leading its current development.

UCB has filed simultaneous UK initial patent applications covering **bicyclic derivatives** (GB0718570, **tropanes** (GB0718571) and **cyclic amino derivatives** (GB0718572). The probability is that this is related subject matter, but these seem to be working titles, not obviously corresponding to titles appearing on the Belgian company's recent published applications. However, the first two titles are virtually identical to those on a pair of initial applications filed in mid-February 2007 (GB0703447 and GB0703450), as noted by Thomson Scientific patent analysts at the beginning of April.

Valetta Health has filed (GB0718543) to protect **urocanic acid derivatives**. Founded in 2002 as part of the Amsterdam BioMed Cluster, the company has the **dermatological and anti-inflammatory uses of 3-urocanic acids (UOPs)** as its focus, based primarily on the work of Professor Jan D Bos at the Academic Medical Center (AMC) from which it is a spin-off. No patent applications have yet appeared naming Valetta Health as applicant, but the University of Amsterdam's **WO0100145**, naming Dr Arthur Kammeijer as inventor, relates to the use of UOPs as free radical scavengers and antioxidants. This case may well now form part of Valetta's intellectual assets, and indeed the name of Prof Bos ("Joannes Dositheus Bos") does appear alongside that of Kammeijer on the corresponding granted US patent.

Applications can be expected to see publication in mid-March 2009.