

Current Patents Gazette

Patenting in Context

News & Highlights from week 0826

This week sees publication of a PCT application from **Achillion Pharmaceuticals** that serves to identify a hepatitis C candidate believed to have been discontinued. As is often the case, there seems to be significance in the timing of the priority documents on which **WO2008076443** is based. The saga began on 18 December 2006, when a single page was filed outlining the synergy achieved *in vitro* when **ACH-806** was combined with interferon, **VX-950** (Vertex's **telaprevir**) or **NM-107** (Idenix's **valopicitabine** metabolite). Then on 08 February 2007 the company put out a press release announcing that, with licensee **Gilead Sciences**, it was discontinuing development, citing raised serum creatinine levels observed in a phase Ib/II trial. Having put that information into the public domain, Achillion went ahead two weeks later and filed a full 36-page document, detailing the biological results, and including in the claims six further thioureas that could be used in similar combinations. Essentially that is the document now published by WIPO, based on a December 2007 final application. So from this it seems that just as Achillion was taking the difficult decision to stop the phase II work on ACH-806, which had shown promise *in vitro*, considerable scientific and administrative effort was going into securing patent protection for its use in antiviral combinations. Incidentally, although telaprevir seems to be progressing well in phase III trials, development of

valopicitabine was discontinued in September 2007, and the NM-107 metabolite is said to be subject to patenting difficulties. In consequence, valopicitabine itself is now the subject of an **Idenix** development program known as **NV-08**, aimed at identifying antivirals from other classes that could usefully be administered in combination. It is even possible that Achillion knew of the difficulties with valopicitabine, when choosing to cover its combination with ACH-806 in the original December 2006 priority document, although the Idenix announcement was not made until September 2007. Whatever the truth behind these observations, the timing of patent applications often tells us as much about the applicant's real motivation as the specification itself.

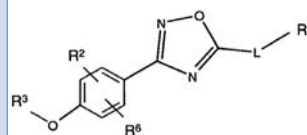
Varleigh has filed GB0809279 with claims to a **histamine-binding protein**. This follows a couple of months after publication of two very similar PCT applications, **WO2008029167** and **WO2008029168**, with claims to the use of the MAPK inhibitor **EV-576** in peripheral nervous and respiratory disorders respectively. This 150-amino acid tick protein, otherwise known as OmCI, was the subject of a January 2007 *J Biol Chem* paper in which the Varleigh inventor, his affiliation given then as **Evolutec Group**, collaborated with workers at **Cardiff** and **Oxford Universities**. In the context of developing **rEV-131**, Evolutec

in March 2008 announced that it has licensed IP rights to Varleigh. Development of this recombinant histamine-binding protein was reported to have been discontinued in December 2006, but a licensee was being sought; the present application may well indicate that the so-called vortucalis allergic rhinitis product is now being progressed by Varleigh.

Proximagen has filed GB0809101 with claims to **dopaminergic compounds**. Background to this new invention may well be found in a handful of published PCT applications in the name of **Proximagen Neurosciences**, the first pair filed in February 2005 (**WO2006087577**, etc) and the remainder a year later (**WO2007091017**, etc). Though the earlier cases were concerned with peptides involved in dopaminergic mechanisms, attention then turned to small molecule dopamine receptor modulators, based on modified amino acids. The company, based on the Guy's Campus of **KCL**, reports several such

compounds in preclinical studies as part of its **PRX-1** discovery program. In a March 2006 press release Proximagen's CEO reported the previous year's performance and included details of the patent filings supporting this and other discovery activity, extending to the **PRX-4** and **PRX-5** programs, the latter relating to D1 agonists described as potent and highly selective.

Veritron has filed a new UK initial application detailing **therapeutic uses of plant extracts** (GB0808974). This follows similar filings from February and May 2007, GB0702780 and GB0710536 respectively. All three applications appear to be related to **WO2006079815**, which claims herbal composition comprising extract of camomile, *Nigella Sativa* or *Acacia Senegal*, stabilised by PVP. The extracts were said to increase cytokine levels such as IL-6, IL-7, IL-8, IL-9, IL-10 and TNF, useful for the treatment of cancer, cardiovascular diseases and immune system decline.



Oxadiazole derivatives are first S1P1 agonists from Abbott.

UK Initial Applications

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A0 applications filed May 15th – May 21st 2008 – expected to see publication in November 2009

- **AcureOmics AB** has filed GB0809105 relating to **biomarkers**, on 19 May 2008. Helpfully, the **Umea University** spin-out issued a press release ten days later giving more detail, reporting that these biomarkers can be used for detection of metabolic, inflammatory or growth changes prior to onset of type 1 diabetes (T1D). Apparently the patent application identifies a number of low molecular weight endogenous compounds that are over-expressed or deficient in subjects at risk for developing T1D. It also reveals that workers at **Lund University** and the **Swedish University of Agricultural Sciences** contributed. AcureOmics itself does not seem to have filed patent applications previously, but almost certainly has access to some of the IP generated over the past three decades by Lund's Professor Ake Lernmark. One of his earliest cases was filed by **Nordisk Insulin**, but he later became associated with **Diamyd Medical AB**, **Apodemus AB**, and the **University of Washington**.

- **Advanced Biomedical** has filed a patent application (GB0809103) with the apparently truncated title "**Aromatic affected**". The Oldham-based company, known commercially as **ABL**, includes former **University of Manchester** spin-out **BioRite**, and specializes in manufacture of peptide and lipid products. Technologies include the **Bioburst** drug and diagnostic delivery platform. It is not immediately clear how this latest invention fits into the company's portfolio, although it does seem to be a sequel to (or more likely a re-filing of) one bearing the same strange title filed on 23 March 2007.

- **Antisoma** has filed an application (GB0808956) for **biological materials and their uses**. Probably linked to the similarly entitled **WO2007034210**, the EP equivalent of which **EP1926750** was recently published on June 04 2008 shortly following the current application. The PCT relates to HMFG1 antibody molecules which selectively bind to a specific target wherein the antibody molecule is modified in its

glycosylation site. Antisoma, based in west London, specialize in developing novel anti-cancer drugs and has published many international patent applications in the field of cancer therapy.

- **Crusade Laboratories** has filed an application (GB0800907) relating to the **infection of cells by Herpes simplex virus**. Crusade, founded in 1999 in Glasgow based on research by Professor Moira Brown and her team at the **MRC** and subsequently at the **University of Glasgow**, specializes in treating cancer using modified Herpes simplex viruses. The company has filed several patents since about 2003 on this topic and is currently carrying out clinical trials on HSV1716, a modified oncolytic virus for the treatment of recurrent glioblastoma multiforme. The current application may relate to a mutant form of HSV1716 or HSV1 virus which may have been modified to act as gene therapy vectors.

- **Myotec Therapeutics** has filed a second UK application covering a "**new therapeutic use**" (GB0809028), following similar claims noted in GB0804454 from March 2008. The company, established in November 2006 with registered offices in Cambridge, was spun out from **Imperial College** employing the expertise of Professors Stefan Anker and Andrew Coats in drug repurposing. The initial focus appears to be cachexia. Probable links to claims by Anker in **WO2007083119** to the use of statins, particularly **simvastatin** or **atorvastatin**, to promote weight gain, skeletal muscle mass increase and treating cachexia

- **Shire** has lodged a cluster of eight new applications with the UK intellectual property office covering **substituted quinazolines** (GB0808947, GB0808948, GB0808950, GB0808951, GB0808952, GB0808953, GB0808967, GB0808968). These are probably related to a series of quinazoline based PDE3 and platelet aggregation inhibitors claimed for potential in thrombosis and

myeloproliferative disorder in **WO2008065444** and **WO2008065445** published on June 05 2008, a couple of weeks after this cluster was filed. The compounds disclosed were 3-substituted anagrelide derivatives. Previously Shire had licensed anagrelide, a quinazoline derivative phosphodiesterase inhibitor, from **BMS** and launched the drug for thrombocytopenia and other myeloproliferative disorders. The company now appears to be investigating **SPD-535** as a platelet-lowering agent with potential for hematological disorders. Related quinazolines have also been disclosed in **WO2006017822** and **WO2006017823**.

- **The Foundation for Innovative New Diagnostics (FIND)** has filed an application (GB0809039) to protect **biomarkers for staging human African trypanosomiasis patients**. This Swiss organization specializes in improving the quality of life of people suffering from poverty-related diseases in the developing world and concentrates its research on malaria, tuberculosis and sleeping sickness. FIND has an ongoing program to develop a serological method of trypanosomiasis diagnosis based on either antibody or antigen detection that will be specific and sensitive enough to guide drug treatment. FIND is currently working with the **Seattle Biomedical Research Institute (SBRI)** to apply single chain variable fragment (scFv) antibody engineering technology in the development of optimized antibody probes for trypanosome antigens in blood.

- **The Katholieke Universiteit Leuven** has disclosed **gene signatures** in a recent application (GB0809069). The university has carried out a clinical trial to identify mucosal gene signatures predictive of response to **infliximab** (a chimeric monoclonal antibody used to treat autoimmune diseases) in patients with inflammatory bowel disease using high-density oligonucleotide arrays which was completed in February 2008. Patrick Neven, an

associate professor in the Biomedical Sciences Group, and his team have published an article about gene signatures in *Lancet Oncology* in March 2008. It is suggested that the current application relates to gene signatures in the diagnosis of cancers.

- **The University of York** and two individual applicants has filed an application (GB0809091) concerning **enhanced glycosylation with mutants of endohexosaminidase A (Endo A); endohexosaminidase glycosynthases**. Fairbanks and Heidecke have previously been associated with the **University of Oxford's** Department of Chemistry, in particular Fairbanks has been named as an inventor on several applications from Isis Innovation, a spin off company from the University of Oxford. Recently they have both published a paper discussing endohexosaminidase-catalysed glycosylation with oxazoline donors: fine tuning of catalytic efficiency and reversibility in Chemistry, June 2008.

- **Univ Northumbria** has filed a new UK initial application covering a **single use drug delivery device** (GB0808969). This appears to relate to the work of Chris Holden, a third year design student, which won the **NPSA** (national patient safety agency) award from the **RSA** (Royal Society for the encouragements of Arts, Manufactures and Commerce). The "**MediDome**" design comprises a soft flexible plastic dome, pre-filled with a measured dose, while the aesthetics show a less threatening form. Adhesive, anesthetic and antiseptic wings allow the device to be attached to the injection site and on depression of the dome a concealed needle is punctures the drug reservoir and guided to administer intramuscular or subcutaneous injection. On release, the needle becomes locked preventing further use. The University is currently seeking funding to develop and commercialize the MediDome device. A second product, the Absorption MediDome, is being considered for the needleless administration of painkillers and certain antibiotics.