

Institute of Research, Washington, DC, USA) showed that MSI1361 kills the intra-erythrocytic stages of *Plasmodium falciparum* *in vitro* by lysing the infected red cell [Kaplan, R.M. *et al.* A novel class of steroids isolated from the dogfish shark (*Squalus acanthias*) induce a reversible spherocytosis in normal erythrocytes and kill erythrocytic stages of *Plasmodium falciparum* by inducing lysis of infected erythrocytes. *American Society of Tropical Medicine and Hygiene Meeting*, 7–11 December 1997, Lake Buena Vista, FL, USA, Abstract].

Several of the aminosterol analogues exhibited potent and selective effects on

human T lymphocytes. 'These were subsequently evaluated in animal models of asthma and found to be surprisingly effective', but, admits Zasloff, 'the aminosterol identified as our lead in asthma still requires optimization'. Ideally, a molecule for this indication should be orally available and work is being conducted to improve this property.

Future prospects for aminosterols

Zasloff is optimistic about the development of all the aminosterols so far described. 'All of them show such potent activity that we expect to develop several useful drugs. I think this may be the most

significant discovery of a novel class of compounds from animal tissues since the prostaglandins; the aminosterols could turn out to be just as important.'

REFERENCES

- 1 Rao, M. *et al.* Aminosterols from the dogfish shark *Squalus acanthias*. *J. Nat. Prod.* (in press)
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Kathryn Senior

E-commerce turns to PriceWaterhouseCoopers

In April 2000, PriceWaterhouseCoopers (PWC; New York, NY, USA) and Ventro Life Sciences (Uxbridge, UK) announced an alliance to create the leading online supplier for laboratory equipment and supplies for the pharmaceutical/biotechnology markets in Europe. The market is currently estimated to be worth US\$7–8 billion. According to Fergus Byrne, PWC's Global Head of Pharmaceutical Consulting, the average major-league pharmaceutical company spends US\$250–350 million to meet its laboratory needs. E-commerce for the life science market seems to be developing into a two-horse race between Ventro – known more widely by the name of their US operating company Chemdex (Mountain View, CA, USA) – and their competitor SciQuest (Research Triangle Park, NC, USA), which has a very similar business model and target audience.

Ventro has turned to PWC for expertise in many areas such as tax, e-commerce regulations and regulatory

compliance. According to Derek McCall, Vice President of Ventro, 'There is a tremendous depth of expertise within the PWC organization that will basically allow us to accelerate the rate at which we can bring this solution to market.'

The Internet is forecast to change the way life science business is performed in Europe – these changes have already happened or are happening in the USA. McCall claims that through the use of an e-procurement solution, pharmaceutical companies could achieve economies of 10–40% in terms of unlocked time, improved purchasing decisions and other benefits.

Ventro already serves the vertical life science marketplace with 1.3 million products listed, 2200 suppliers and 24,000 users (company annual report). Revenue for the Q4 of 1999 was \$20 million. The company also operates in three other vertical healthcare and industrial marketplaces, namely specialty medical products, process plant supply and healthcare supply.

e-Mission

Ventro specializes in B2B (business-to-business) e-commerce in vertical marketplaces and its corporate mission is to create value on both sides of the supply chain – both for the supplier and for the user enterprise organization. Constraints around B2C (business-to-consumer) e-business are well understood – notably, the poorer penetration of the PC into the home in Europe relative to the US, and the far greater connection and online charges. According to McCall, in the B2B arena, these constraints do not apply, and some projections suggest that Europe could even overtake the US in B2B, with the UK and Germany identified as hotspots for hypergrowth in the next two years.

Scaleable solutions

Typically, markets suitable for the Ventro approach have a fragmented supplier base without dominant operators. The top ten life science suppliers

hold no more than 20% market share. Complex market places equate to larger opportunities.

The European marketplace is also much more complex than in the US, the latter finding benefiting from a common currency, common language, common supplier base and generally larger, central research centres. In addition, the supply chain in Europe today is inefficient; several players (e.g. regional resellers) can be involved between the supplier and end-user of a product. At the same time, end-user processes are usually fragmented, with users failing to capture the right information concerning what is used and who supplies it.

Ventro aims to provide a one-stop shop solution by bringing suppliers' products together in a single searchable database with intuitive and sophisticated search capabilities. For large pharmaceutical companies, this will mean providing highly customized solutions that integrate procurement

application solutions. Contract pricing with specified suppliers or the use of selected lists of suppliers will be incorporated, for example. For the rapidly expanding numbers of smaller biotechnology and start-up companies, the solution will be less customized and will remain hosted by Ventro.

There are several advantages to ordering products via such a centralized resource. Information is provided in real time, so pricing and stock availability data should be accurate. This method makes comparison of product specifications easy and enables more specialized products to be made more widely available. It is also possible to eliminate maverick purchasing – buying outside of agreed arrangements between suppliers and the company.

However, building the infrastructure to supply complete end-to-end solutions is no small undertaking. The Chemdex operation currently employs some 60 PhD qualified individuals to

ensure that requirements and challenges of supplier and end-user are fully understood.

Growth strategy

Having established the technology platform, operational expertise and economies of scale, McCall believes Ventro is poised to expand rapidly in the course of the year 2000 into other marketplaces. Originally, in the US, it took 17 months and US\$60 million before Chemdex achieved its first transaction. For example, the first transaction for the second venture, Promedix – focusing on speciality medical products and services – took place after only four months. Expansion into new marketplaces is expected to be even more rapid. At present, Ventro operate in four industry-specific marketplaces, but by year end, they expect to be operating in a further six.

David Hughes

Gene therapy alternative to HAART for HIV

HIV infection could be treated using gene therapy in the future, to inhibit activation of the latent virus. A team based at The Children's Hospital of Philadelphia (PA, USA) has shown that inserting the *antitax* gene into blood cells from infected patients can inhibit the replication of HIV-1 (Ref. 1).

The prognosis for infected individuals has improved over the past few years with the introduction of highly active antiretroviral therapy (HAART), a combination of drugs that decreases HIV replication to undetectable levels in many patients, confining the virus to a latent state. However, HAART presents serious problems. Treatment is

expensive, difficult to follow and might have to be taken for life, and the side effects include loss of appetite and increased vulnerability to other infections. Recent studies have shown that latent HIV-1 infection persists in the CD4⁺ T lymphocytes even in HAART patients with well-controlled viral replication, and these cells decay very slowly². If treatment with HAART is discontinued, the reservoir of latent virus can re-emerge as an active infection³.

Involvement of TAT in HIV

A viral protein called TAT is a key target for any potential genetic intervention in HIV replication. Produced by

the *tat* gene, TAT is involved in the expression of all HIV genes by interacting with a viral RNA sequence called the *tat* activation response element (TAR)⁴. It is also involved in the pathogenesis of AIDS by activating the expression of inflammatory cytokines, some of which (e.g. TNF α) are promoters of HIV replication⁵. TAT is therefore essential for HIV-1 replication and important in the transition from latent to active infection¹.

The Philadelphia team used an artificially designed antisense gene called *antitax* to inhibit TAT. Antisense molecules are RNA strands that bind to complementary mRNA from the target