GEN Biobusiness

State of Industry Discussed at BIO-Europe

Global Progress of the Biotech Sector and Challenges to Be Faced Addressed at Meeting

Susan Aldridge, Ph.D.

Nearly 1,500 delegates from pharma, biotech, and the investment community attended "The 11th BIO-Europe" meeting. Sponsored by EDB Group and recently held in Dresden, Germany, it resulted in over 5,000 one-on-one meetings.

A panel of leading figures from the German, U.K., and U.S. bioindustry discussed the challenges facing the biotech sector, both in Europe and globally.

Speaking for the host nation, Peter Heinrich, Ph.D., CEO of **Medigene** (www.medigene.com) and president of BIO Deutschland (www.biodeutschland.org), said that the government must do more to attract investors and ensure continuity of finance for companies. There is also a need for more mergers to attain the critical mass the biotech sector requires. "A German biotech scene," he stated, "that is no more than a patchwork will not lead to success."

In terms of innovation, pharmaceutical pricing differences mean that the U.S., where prices are higher and companies are richer, is effectively subsidizing R&D for the rest of the world, said Jim Greenwood, president of BIO. "Increasing prices in Europe might increase innovation."

Biotech in the U.S. vs Europe

Jim Mullen, chairman and CEO of **Biogen Idec** (www.biogen.com) and chairman of BIO, looked at reasons why biotech seems to have grown disproportionately in the U.S. compared to Europe. Funding from NIH has put a firm foundation under the science and there are strong mechanisms to allow transfer of IP from academia to the private sector. In Europe, however, there is more of a cultural barrier to the academia-private sector connection.

There is also a strong VC community in the U.S., where as in Europe, pricing policies mean that the rewards for such investors in biotech are not so great.

U.K. biotech has more than 50 products in late-stage clinical development and the government is supportive, pointed out Simon Best, chairman of **Ardana Bioscience** (www.ardana.co.uk) and chairman elect of the BioIndustry Association in the U.K. However, a major problem is to get the National Health Service to be more innovative in its use of new products.

Despite the challenges, there are still significant deals to be made. Already, Global Life Science Ventures (GLSV) has invested in around 30 European companies and led 10 companies to IPO in Europe and the U.S., including, this year, **Intercell** (www.intercell.com) raising €47 million and **Coley Pharmaceuticals** (www. coleypharma.com) raising $96 million to IPO.

Also, another GLSV company, **GlycArt** (www.glycart.com), was acquired in a trade sale by **Roche** (www.roche.com).

VCs want to see validated proof-of-principle for drug candidates, a solid business model, experienced management with product development expertise, and a focus on products. "We are looking for novel approaches in unmet medical need, where we can finance to the next important value increase, as the lead investor," said Holger Reithinger, Ph.D., principal at GLSV.

An example is the recent investment in **Neuraxo** (www.neuraxo.com) that has a preclinical therapy for acute spinal cord injury, which currently has no cure.

Solvent extraction during downstream processing of one of the anticancer drugs that IRL Biopharm makes by fermentation.

The GLSV team recently performed a survey of nearly 100 European biotech executives, analysts, and investors that showed 57% of biotech respondents view the market as undervalued. Respondents believe that lack of finance and inability of companies to take innovation to the marketplace are bigger hurdles than regulatory and safety issues.

Of the respondents, 87% see the long-term prospects for the biotech sector as favorable and 46% of respondents are more optimistic about the future of the biotech sector in Europe than they were a year ago. Filling pharma's R&D pipeline and developing therapeutics for unmet medical need are seen as the greatest value drivers. Also, 87% of investors and analysts recommend investment in biotech, although with some reservations.

Cancer Therapies

New cancer drugs are always going to be of interest to VCs and developments in clinical trials, such as the use of biomarkers as surrogate endpoints, could help progress therapies to market.

Glen Clack, M.D., oncology research physician at **AstraZeneca** (www.astrazeneca.com), described the use of two biomarkers, both collagen breakdown peptides, in bone cells in the development of a first-in-class orally active kinase inhibitor that blocks invasion of the cancer. These drugs are particularly interesting, said Dr. Clack, given the failure of MMP inhibitors.

"New imaging technologies and biomarkers are incredibly helpful for proof-of-concept," said Jörg Möller, vp global clinical development, **Bayer HealthCare** (www.bayer.com). "But," he continues, "for later stages of development, we will stick with measuring tumor diameter."

He also discussed the relative advantages and disadvantages of progression free survival (PFS), a surrogate endpoint in cancer trials, compared with five-year survival. In the U.S., PFS can be used for accelerated or full-approval of an anticancer drug, but the EMA is not so keen. "There is room for improvement in getting harmonization on this," he added. "New modalities, such as biomarkers and imaging, are good for hypothesis generation but need more validation."

Andrew Stephens, M.D., Ph.D., director of oncology scientific affairs at **OSI Pharmaceuticals** (www.osip.com), also talked about the use of biomarkers in trials of Erlotinib, which is used in the treatment of non-small-cell-lung cancer. "One must be cautious about interpreting small, uncontrolled trials if the endpoint is a biomarker," he cautioned.

Finally, Agamemnon Epenetos, Ph.D., CEO of **Somanta** (www.somanta.com), discussed the use of imaging associated with HER-2 and MUC-1, a pan-cancer marker, to select patients for cancer treatments.

The company is also looking at hypoxia, a feature of most tumor tissue that tends to create resistance to all forms of treatment. Plasma osteopontin can be used as a biomarker of hypoxia to show which patients might benefit from Prodrax, a family of hypoxia-activated pro-drugs that Somanta is developing. "This approach turns the tumor's strength into its weakness," explained Dr. Epenetos.

Cancer therapy is also the focus of **IRL Biopharm** (www.irl.cri.nz), a company making microbial toxins for chemotherapy to be used either alone or as a "payload" to an antibody or other conjugate. The company developed processes that allow the fermentation of marine organisms requiring high salinity that have previously been hard to exploit. Besides contract research, IRL Pharma is also creating its own library of microbial toxins.

Another New Zealand company, **Pacific Edge Biotechnology** (www.pacificedgebiotech.com), a spinout of the University of Otaga, is developing microarray-based diagnostics and prognostic tests in bladder, gastric, and colorectal cancer. These are intended for early diagnosis, monitoring for recurrence, and screening populations.

The bladder cancer assay, based on mRNA profiling of three susceptibility genes, is currently in clinical trials in Japan. "The bladder cancer test has elucidated some pathways to work on," said David Darling, CEO.

The company is currently selecting Mabs for the ELISA-based gastric cancer test and hopes to get it into the clinic within a year.

The Korean Biotech Industry

Besides the significant New Zealand presence at BIO-Europe, there was also a large delegation from the Republic of Korea, reflecting the global nature of the biotech industry. As the tenth largest economy in the world and a member of the Organization for Economic Cooperation and Development since 1996, Korea is proving to be an attractive environment for foreign investors.

Woo-Suk Hwang, Ph.D., professor at Seoul National University, focused the world's attention on Korea when he reported the first-ever cloning and extracting of patient-specific embryonic stem cells in 2004, followed by the first cloned canine in August, 2005.

Korea has a particularly strong IT infrastructure, with the highest penetration of broadband in the world, that has helped kick-start biotech, especially in the areas of genomics, proteomics, and bioinformatics. The industry has been growing for the last 10 years, underpinned by strong government support. Since 1998, its R&D investments has increased in the sector to $708 million.

Currently, over half the Fortune 500 countries have a presence in Korea. The government has several initiatives under way to further improve the investment environment.

Korea has a good track record in biologics manufacturing and is becoming well-known for high quality clinical trials. The biotech industry is being organized around four regional clusters and 25 centers of excellence.

Also, its strategic location, between China and Japan, provides a gateway to the Asian pharmaceutical market, worth $83 billion and growing rapidly. The Korean pharmaceutical market alone is the tenth largest pharmaceutical market in the world.

There are some significant examples of foreign direct investment. In 2002, **Berna Biotech** (www.bernabiotech.com) acquired Korean Greencross Vaccine in a deal with Rhein Biotech and a further $10 million investment was made in April, this year.

Meanwhile, **Celltrion** (www.celltrion.com) was created in 2002 as a joint venture between **Vaxgen** (www.vaxgen.com), a U.S. biotech firm, and Korean investors, leading to the establishment of what will be Asia's largest biopharmaceutical facility.

Another company, **ViroMed** (www.viromed.com), was founded out of Seoul University, and **Takara Bio** (www.takara-bio.co.jp) acquired a 50% stake for $6 million. The company, which is focused on cardiovascular problems, cancer, and genetic disorders, initiated Korea's first gene therapy trial in 2001.

Finally the Korean subsidiary of **Eli Lilly** (www.lilly.com) was formed in 1998 from a joint venture with Daewoong Pharmaceuticals and now has a manufacturing and a sales and marketing operation.

One of Korea's most promising companies is **Immunomics** (www.immunomics. com), which is involved in immunotherapy for autoimmune diseases and cancer. It has IP on therapeutic antibodies, immunomodulatory targets, stem cell therapies, and stem cell media. Most of its pipeline products are in Phase I, with NDAs projected for 2007/8.

The company has various collaborations with organizations, such as the Immunomodulatory Research Center in Ulsan. "We want to be the leading Asian company in immunotherapy and clinical trials, within ten years," said Byoung-Se Kwon, Ph.D.

Antifungal Applications

European companies were well represented at the meeting and many had news of recent developments. For instance, **BioAlliance Pharma** (www.bioalliancepharma.com) is a drug delivery and small molecule company, focused on overcoming treatment resistance in fungal infection and cancer. It recently filed for EU approval of Miconazole Lauriad™ for treatment of oral candidiasis.

The product uses the company's adhesive technology to formulate the antifungal into a tiny patch applied to the surface of the upper gum. This should improve compliance compared to existing local formulations and provide an alternative to systemic antifungal treatments, which can lead to resistance. The FDA has allowed an IND for a Phase III trial, in HIV-induced oral candidiasis that will start in 2006.

The oral candidiasis market, covering those with cancer, HIV, or otherwise immunocompromised patients, is worth around €330 million, according to Richard Keatinge, Ph.D., vp business development. BioAlliance Pharma hopes to capture a significant part of this, if the advent of Miconazole Lauriad persuades physicians to switch from systemic to local treatment.

The company also just completed a Phase I trial of a follow-on product, acyclovir Lauriad, for oral herpes. BioAlliance Pharma's other platform is the Transdrug® nanoparticle technology that is being used to deliver the anticancer drug directly to cells, overcoming resistance.

Doxorubicin Transdrug® has orphan drug status in the U.S. and the EU and has shown promising preliminary results in a Phase I/II trial in France for hepatocellular carcinoma.

Hybrigenics (www.hybrigenics.com) is completing a transition from being a technology platform company to one with a dual business model. Fee-for-service work on protein-protein interactions utilizing an optimized yeast 2-hybrid technique is being used to generate revenue to finance in-house oncology drug development.

Its most advanced program, currently in preclinical development, is focused upon the ubiquitinylation pathway that controls the protein level in cells. **Millennium's** (www.mlnm.com) multiple myeloma drug Velcade® (bortezomib) also inhibits this pathway, but the Hybrigenics' compounds work at the upstream end and should be more specific in their mode of action. GEN

Hybrigenics is developing oncology drugs based on inhibition of the ubiquitinylation pathway.