

Contents

Editorial

[Mobilisation French style](#)

France

[Sector-wide fund for biotech](#)

The stock market, fundraising and milestones

[TopoTarget moves to raise funds](#)

[New milestone for Galapagos](#)

Agreements

[Genzyme finalises transaction with Bayer](#)

Benelux

[New Flemish consortium set to scrutinise the brain](#)

Industry and partners

[mGluR5 now a target in multiple indications](#)

[Third indication unveiled for Affiris vaccines](#)

Clinical trials

[A novel approach in Parkinson's disease](#)

Products

[Arzerra®: another step towards marketing authorisation](#)

[Cerepro®](#)

In brief

[Lonza moves into the breach](#)

[Hybrigenics](#)

[ACR16 = pridopidine](#)

New functionalities on the *BioPharmaceutiques* website!

A number of new functionalities are now available on the *BioPharmaceutiques* website, in order to help you search through the European deals listed in our summary tables. As with the Clinical Studies table (where searches can be performed by Phase (I, II, IIa, IIb, III), company, compound, disease or status (launch or result)), we now offer you the ability to select agreements by type: R&D, licence, production, commercialisation/distribution or marketing/promotion. Check it out at <http://www.biopharmaceutiques.com/en/tables/agreements/>

Editorial

Mobilisation French style

Will France seize its opportunity and fully embrace the biotechnology initiative presence over the last two decades, but which has continually faltered due to lack of adequate and concerted political, scientific and industrial commitment? The recent announcement made by the French Strategic Investment Fund (FSI) concerning the launch of its very first sector-wide initiative in the biotechnology field nevertheless demonstrates a degree of determination to mobilise public funds in favour of this sector ensuring not only promising

opportunities for development but also much-needed and healthy independence through the creation of an investment fund rather than simply providing aid or subsidies. Behind this desire to invest we may discern an affirmation of the strategic dimension of this young industry in which France undeniably enjoys a number of advantages. Although it is unrealistic to expect the FSI to fulfil this role single-handedly, it nevertheless appears well-placed to provide a platform for supervised and pragmatic collaboration of the actions undertaken jointly by the public authorities and pharmaceutical and biotechnology manufacturers.

Anne-Lise Berthier

France

Sector-wide fund for biotech

The creation of an investment fund for the biotechnology sector has become a reality in France. A major step forward has been taken with the announcement of partnerships between the French Strategic Investment Fund (FSI) and France Biotech and OSEO (see *BioPharmaceutiques* No 106). Following yesterday's invitation by France Biotech to officialise this joint project, FSI Director General Gilles Michel indicated that "there are plans to set up the fund by the end of July". Although the French pharmaceutical firms invited to co-invest have not yet indicated how much they intend to spend, Gilles Michel considers that the total sum will be between EUR 100 m and EUR 150 m, "with the idea being to trigger an environment of encouragement for investment.

Three modes of intervention. While the sums involved clearly appear insufficient, the launch of this sector-wide initiative nevertheless marks official recognition of the strategic importance of the sector for the French economy. Such recognition is vital for French biotechnology, which although moving forward with a portfolio of 158 drugs currently in development in some 50 companies, nevertheless experienced a massive 79% drop in investment in 2008 (see *BioPharmaceutiques* No 98). In practice, this biotech fund will be granted FCPR status (high-risk placement fund) and will be managed by the FSI. The latter will invest up to EUR 2 m to the project as a co-investor alongside drug companies and public and private investors. The mode of operation of the FSI possesses three major characteristics: minority investment followed by withdrawal after five to seven years, accompaniment of industrial projects, and a place on the board of the firms being accompanied. Although this biotech fund is not concerned with start-ups, it will target SMEs directly or indirectly involved in the preclinical and clinical development of innovative health products as well as companies offering scientific or technological platforms or services. The partnership with France Biotech will assume its full meaning in terms of choice of targets by making the measure known to French biotech firms and assisting with identification by the FSI of extremely promising companies.

Finally, support of biotechnology companies and by the FSI will also take two other forms. Ongoing activities will be strengthened through CDC Entreprises, the 20 affiliated funds of which have invested EUR 295 m in 152 biotech SMEs over the last six years. Additional efforts are to be made regarding these funds, with the FSI expected to contribute EUR 75 m over the next two years. Last but not least, while the duration of investment to be made by the biotech funds are already based on the longest development periods for the development of healthcare products, the FSI can also act directly for investments lasting ten years. In this case, the sums may exceed EUR 10 m for a maximum of two to three projects a year.

The stock market, fundraising and milestones

TopoTarget moves to raise funds

TopoTarget is seeking to improve its cash balance through a public offering of new shares expected to raise between DKK 57.4 m and 120 m (EUR 7.7 m to 16.1 m). At best, the Danish company's cash position will triple from the fairly low position of DKK 61.4 m (EUR

8.2 m) at the time of publication of the offer compared with DKK 108 m (EUR 14.5 m) on 31 December 2008. TopoTarget's last round of fund raising totalling EUR 48.4 m was completed two years ago in order to purchase Swiss company Apoxis (see *BioPharmaceutiques* No 19). Given the current economic climate, the company's ambitions are now more modest; the aim is to secure sufficient resources in 2011 to achieve its key objectives regarding the development of candidate drugs in its pipeline. The priority remains the completion of an ongoing phase III for its most advanced product, belinostat (histone deacetylase inhibitor) in the treatment of peripheral T-Cell lymphoma, as well as furthering development in other indications so as to increase its value with a view to a partnership agreement (see *BioPharmaceutiques* No 101).

Pre-emptive shareholder rights. This rights issue, announced at the presentation of the company's financial results for the first quarter of 2009, was authorised by shareholders at the extraordinary general meeting held on 27 May. The company's General Director, Peter Buhl Jensen, resigned from the board immediately prior to publication of the offering. Existing shareholders will be allotted pre-emptive rights for the new shares, with one share to be purchased for each share held. The shares have a nominal price of DKK 1 and the subscription price is DKK 2. The issue will open on 16 June and end on 29 June. Pre-emptive rights can be traded on Nasdaq OMX Copenhagen from 11 to 24 June. As the company's financial position weakens, it could find itself becoming a takeover target. The TopoTarget board stated last month that it had been approached by a listed biotech company from outside Denmark regarding a merger in the form of a share exchange, but that the administrators felt that the offer was not sufficiently attractive, at least for the moment.

New milestone for Galapagos

To date, Belgian firm Galapagos has received more than EUR 10 m in staggered payments from Janssen Pharmaceutica as part of a partnership agreement between the two companies set up in October 2007 concerning the development of candidate drugs for the treatment of rheumatoid arthritis. The latest payment of EUR 3.4 m comes after successful completion of an additional stage concerning optimisation of medicinal chemistry using one of the company's programmes. Following the signature of the agreement, two staggered payments were made in January 2008 and January 2009. The first, totalling EUR 3.4 m, was associated with GT146, one of Galapagos' most advanced programmes, while the second, of EUR 3.75 m, was made after demonstration of the ability of one of the compounds developed against targets identified by the Belgian biotech company biotech to reduce an inflammatory disease biomarker in inflamed joint tissue cultured from collagen-induced arthritic mice. In conclusion, following the initial partnership drawn up between Galapagos and Janssen Pharmaceutica in March 2007, the two companies are now involved in two major agreements (See [Summary Table of Agreements](#)). In addition to this agreement in the field of rheumatoid arthritis, which provides Janssen with the option of acquiring worldwide licences for up to 12 in-house Galapagos programmes, the two companies are now working on the identification of oncology targets. In addition, Galapagos has just announced the appointment of Solvay Pharmaceuticals CEO Werner Cautreels as an independent director on its board until the next general shareholder assembly in 2010.

Agreements

Genzyme finalises transaction with Bayer

Genzyme and Bayer Healthcare have finalised a strategic agreement less than two months after the announcement of this transaction which will see Genzyme recover its worldwide rights for Campath®/MabCampath® (alemtuzumab) in oncology while maintaining all rights for monoclonal antibodies in multiple sclerosis (see *BioPharmaceutiques* No 102). This operation, which has now received the blessing of the regulatory authorities, marks the effective extension of Genzyme's product portfolio into oncology-haematology with the acquisition of Campath®, Fludara® (fludarabine phosphate) and Leukine® (sargramostim - recombinant G-CSF). In addition, the EMEA Committee on Medicinal Products for Human Use has issued a favourable opinion concerning the use of Mozobil® (pierixafor - a CXCR4 chemokine receptor antagonist) in combination with G-CSF (granulocyte-colony stimulating

factor) to enhance mobilisation of haematopoietic stem cells in patients with non-Hodgkin's lymphoma and multiple myeloma was a view to future autologous transplantations. This product was granted orphan drug status in this indication in October 2004 in Europe and has been authorised in the United States since last December.

Benelux

New Flemish consortium set to scrutinise the brain

The Flanders Institute for Biotechnology (VIB), the Interuniversity Microelectronics Centre (IMEC) and the Catholic University of Leuven are to join forces as part of an interdisciplinary research initiative combining nanoelectronics and neurobiology. This two-fold approach will allow researchers taking part in the project to study the biofunctional mechanisms of neurones with unparalleled precision.

In practice, the initiative will involve the creation of an interdisciplinary research centre, known as NERF (Neuroelectronics Research Flanders), to be located within the IMEC facilities. IMEC, a non-profit making association set up 25 years ago by the Flemish government with an initial investment of EUR 2 m, is now the most important European research centre in nanoelectronics and nanotechnology, with an annual budget of around EUR 250 m and 1 650 staff from more than 55 countries. The new centre, which is far more modest, is expected to have 50 researchers of international renown on its books by 2014. While receiving funding of EUR 3 m from the Flemish government, it will be financed equally by the three founding bodies.

The activities NERF lie at the interface between biology and electronics, and its aim will be to increase knowledge concerning the neuronal circuits to establish new research methods, new tools and new diagnostic and therapeutic approaches regarding disorders of the central and peripheral nervous systems. The scientific committee will meet for the first time on 29 October to define the road map.

Industry and partners

mGluR5 now a target in multiple indications

Swiss firm Addex Pharmaceuticals, which specialises in allosteric modulation of metabotropic glutamate receptors type 5 (mGluR5), with three products developed in four indications, will now have to contend with increasing competition in this area from major pharmaceutical companies. One of its products, ADX63365, an mGluR5 positive allosteric modulator developed in the treatment of schizophrenia, has already attracted US firm Merck&Co (see [Summary Table of Agreements](#) and *BioPharmaceutiques* No 48). Addex is also hoping to sign an advantageous agreement in 2010 for its most advanced product, ADX10059, a negative allosteric mGluR5 modulator, in phase IIb trials since December in two diseases, gastro-oesophageal reflux (GOR) and migraine (see [Summary Table of Clinical Studies](#)).

Recent scientific congresses have highlighted results obtained with this small molecule. At the recent Digestive Disease Week, in the company presented the results of a phase IIa clinical study conducted in GOR in 24 patients. The study demonstrated the efficacy of one day of treatment with ADX10059 in relation to placebo in reducing the number and duration of episodes of gastric reflux. A study demonstrated the efficacy of ADX10059 versus placebo in reducing the number (2 with the Addex product versus 7 with the placebo) and duration (total duration of 5 minutes vs. 14 minutes) of episodes of gastric reflux. These data, initially unveiled in 2007, were first published in a scientific journal (see *BioPharmaceutiques* No 21) **(1)**. Last month, the phase IIa results for ADX10059 in the treatment of migraine attacks were presented at the annual Congress of the American Academy of Neurology.

Increasing interest in Parkinson's disease. Addex is still alone in its work on products targeting mGluR5 in the treatment of migraine, although it will encounter competition from Novartis and AstraZeneca, who are also developing an antagonist of this receptor in the treatment of GOR and in other indications not yet investigated by Addex, mainly fragile X

syndrome (a genetic disease that causes mental retardation) for Novartis with AFQ056 and painful diabetic neuropathy for AstraZeneca with AZD2066. Last November, Novartis published promising phase IIa study data for its product in the mental ated bys receptormy of neurologyo defineent treatment of the levodopa-induced dyskinesias in Parkinson patients. AstraZeneca is also thinking about this indication, for which Addex is open to begin phase II trials on another product at the end of the year, namely ADX48621, another negative allosteric mGluR5 modulator with proven safety in healthy volunteers (see [Summary Table of Clinical Studies](#)).

(1) A proof of concept study evaluating the effect of ADX10059, a metabotropic glutamate receptor-5 negative allosteric modulator, on acid exposure and symptoms in gastro-esophageal reflux disease. C. Keywood and *al.* (2009) *Gut* published on line 20 May 2009; doi:10.1136/gut.2008.162040

Third indication unveiled for Affiris vaccines

After Alzheimer's disease and Parkinson's disease, Austrian company Affiris continues to unveil new indications slowly but surely for its vaccines currently under development (see *BioPharmaceutiques* No 83). The company is also working on a project involving a vaccine against atherosclerosis, again emanating from its Affitome® technology based on induction of an antibody-type immune response against a target associated with this disease, using peptides mimicking the structure of natural epitopes. The target protein in this case is cholesteryl ester transfer protein. By reducing the activity of this protein, the Affiris peptide vaccine should increase concentrations of good (HDL) cholesterol to the detriment of bad (LDL) cholesterol. Development of this vaccine, which is still in the preclinical stages, has received European funding as part of the EuroTrans-Bio joint research programme. This project, lasting thirty months and conducted jointly with German firm EMC microcollections, specialising in combinatorial chemistry, should result in the initiation of clinical trials of the vaccine.

Affiris is not the first European company to develop a vaccinations strategy against atherosclerosis; Swiss firm Cytos also has a candidate-vaccine against this disease in its preclinical pipeline (see *BioPharmaceutiques* No 25). Although based on the Immunodrug® technology also designed to induce antibody-type immune response, unlike Affiris vaccines in which are comprised of peptides, Cytos vaccines utilise virus-like particles to carry antigens.

Clinical trials

A novel approach in Parkinson's disease

Although various therapeutic strategies for Parkinson's disease are currently being studied (cell therapy, gene therapy), Swedish firm NeuroNova has adopted an alternative approach consisting of action on dopaminergic pathways (which are damaged in patients with Parkinson's disease) by direct stimulation of progenitor cells in the brain located near the dopaminergic fibres. The product in question, sNN0031, involves platelet-derived growth factor (PDGF-BB), a natural protein suitable for direct administration inside the cerebral ventricle. The treatment is given by infusion into the ventricle via a catheter and a pump implanted in the patient, which should help reduce the adverse effects associated with systemic administration of growth factors.

Two products in clinical trials. In mouse models of Parkinson's disease, intracerebroventricular sNN0031 has improved symptoms and restored nerve cells. Following approval by the Swedish drug evaluation agency, NeuroNova initiated its first clinical study with this drug in March in order to evaluate safety and tolerability in Parkinson's disease patients. This double-blind, placebo-controlled phase I/II study in two Swedish centres is being performed in 12 patients and is expected to be completed in March 2010. The study protocol involves 2 weeks of treatment and 10 weeks of follow-up, and three different dosages of sNN0031 will be tested. This is the second NeuroNova product to reach the clinical stage. sNN0029 (vascular endothelial growth factor), which is given by direct continuous infusion in cerebrospinal fluid, is currently undergoing a phase I/II study in the

treatment of amyotrophic lateral sclerosis. The study, initiated last December, conducted in Belgium at the University Hospital of Leuven and for which 28 patients will be recruited, is expected to be completed next March (see *BioPharmaceutiques* No 87 and [Summary Table of Clinical Studies](#)).

Products

Arzerra®: another step towards marketing authorisation

Danish company Genmab has made further progress with a favourable opinion from an FDA advisory committee concerning authorisation for Arzerra® (ofatumumab), its anti-CD20 monoclonal antibody developed in tandem with GSK for the treatment of chronic lymphocytic leukaemia in patients refractory to treatment with fludarabine (Fludara®) and alemtuzumab (Campath/MabCampath®). The advisory committee voted 10 against 3 in favour of these oncological drugs. The MA application has received fast-track status and the FDA is expected to make its final decision in the autumn. If successful, this will be the first MA granted for a monoclonal antibody developed by Genmab. Note that Arzerra® is part of a rich clinical programme with ongoing development in a total of 5 indications (see [Summary Table of Clinical Studies](#)). In addition to chronic lymphocytic leukaemia, studies are also being conducted in the treatment of non-Hodgkin's lymphoma, rheumatoid arthritis, diffuse large B-cell lymphoma and multiple sclerosis.

Cerepro®

Following approval by the French authorities at the start of the year, a second European country, Finland, has now authorised named patient supply (NPS) for Cerepro® (sitimagene ceradenovec) from UK company Ark Therapeutics. This authorisation follows submission of an application by a neurosurgeon and should allow a further patient presenting high-grade glioma to receive this "standard" gene therapy based on the suicide gene approach. An EMEA opinion regarding the latest MA application filed in December 2008 is now expected during the final quarter of the year (see *BioPharmaceutiques* No 87).

In brief

Lonza moves into the breach

Swiss company Lonza continues to increase the production capacity in Asia. After Singapore, where CMO is currently building a dedicated factory for manufacturing in mammalian cells and a cell therapy unit, the company is now turning its attention to India (see *BioPharmaceutiques* No 108). Lonza, which for the moment only has a sales office in Bombay, has just purchased a plot of a dozen hectares in Genome Valley in Hyderabad. It plans to invest USD 150 m in the building of R&D and bioproduction units. These operations will be conducted in two phases, and the facilities are expected to be operational within the next 4 to 5 years.

Hybrigenics

Good news for Hybrigenics: revenue from the company's service offer based on its yeast two-hybrid screening technology for the study of protein interactions increased 79% during the first quarter of 2009, rising from EUR 408 000 in Q1 2008 to EUR 730 000 this year. In conclusion, while an initial payment of EUR 400 000 resulted from renewal at the start of the year of its R&D partnership agreement with Servier concerning a ubiquitin-specific protease involved in cancer, the French firm's operating revenue stood at EUR 1.271 m for Q1 2009 (+141%).

ACR16 = pridopidine

The WHO has assigned the international non-proprietary name (INN) of pridopidine to ACR16, a dopaminergic stabiliser from Danish company Neurosearch, currently in phase III trials in Europe in the treatment of Parkinson's disease (see [Summary Table of Clinical](#)

Studies)

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