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AB Science and its partners receive €10m from OSEO

as part of the APAS-IPK project for the development of a new generation of anti-cancer drugs

AB Science SA (NYSE Euronext - FR0010557264- AB), pharmaceutical company specialised in research, development and marketing of protein kinase inhibitors (PKI), **Bull**, specialist in information technologies and particularly high performance computing solutions, **Genomic Vision SA**, biotechnology company specialised in molecular diagnosis, and **Skuld-Tech,** biotechnology company specialised in the discovery of biomarkers and the development of diagnostic tools and companion tests, established formed a partnership for the development of new targeted cancer treatments.

The partnership will carry-out of the APAS-IPK (*Amélioration de la Prédictivité de l'Activité et de la Sélectivité des Inhibiteurs de Protéines Kinases en Oncologie* [Improvement in Predictiveness of the Activity and Selectiveness of Protein Kinase Inhibitors in Oncology]) project, supported by OSEO's Industrial Strategic Innovation (ISI) programme.

OSEO, through its programme supporting Industrial Strategic Innovation, will grant the project a total amount of €10m (including notably €6.2m to AB Science, €2m to Bull, €0.7m to Genomic Vision and €0.3m to Skult-Tech) in the form of repayable advances and subsidies.

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The objectives of the APAS-IPK project are to devise tools to improve understanding of the protein kinase (PK) family and their role in the development of cancers and the acquisition of resistance to treatments, and the provision of new treatments enabling targeted and personalised treatment of patients.

PKs are enzymes involved in the cell signalling paths. They act as regulators of cell function. The unregulated activation of these enzymes, due to mutations for examples, may lead to several forms of cancer.

Inhibition of these proteins is an important area of research in the battle against cancer. Currently the kinase inhibitors on the market or under development are principally competitive inhibitors of ATP, the principal ligand of the kinases. They nevertheless demonstrate a low level of selectiveness explained by a limited functional understanding of these proteins, hence a lack of more specific and less toxic molecules.

The complexity of the proteins, their structures and their mechanisms of action renders the current *in silico* and *in vitro* models insufficiently effective. The major challenge of the APAS-IPK project and the partners involved is to develop high performing and predictive models of the interactions and biological effects of the Protein Kinase Inhibitors (PKI) and to use them to develop a new generation anti-tumour therapy, with a low level of toxicity, targeted and personalised according to patients' predispositions.

AB Science, leader of this project, is focused on the discovery and development of new PKIs in the fields of oncology and inflammatory and neurodegenerative diseases. Its principal molecule, Masitinib, shows anti-tumour effects and can re-sensitise tumours to chemotherapy according to the results obtained in several preclinical and clinical trials.

The large amount of biological data on Masitinib and other PKIs developed by AB Science and the additional data acquired within the framework of the project with the collaboration of the public laboratories of the CNRS and Inserm (U8147 and U891) will feed the creation of *in silico* models developed in partnership with Bull. Moreover, biological samples collected during Masitinib clinical trials will be used to establish companion tests predictive of the therapeutic response of the molecule and the potential associated toxicity (Skuld-Tech, Genomic Vision).

One of the key measures of the project is based on a strategy of innovative and high performing molecular modelling making it possible to access an extremely broad body of information connecting the 3D dynamic structure of the kinases, the stability and specificity of the ligand-kinase complexes and the biological data available.

In order to enable complete and effective *in silico* modelling of the protein kinases and their inhibitors, a very high computing capacity is required. Bull is a French company with a globally recognised know-how in the construction of supercomputers and has the role in this programme of creating a high performance computer (HPC – "High Performance Computing") with an innovative architecture specially adapted to the field of Life Sciences.

UMR 8113 will offer its molecular dynamics expertise in order to improve the modelling of the interactions. Historically, UMR 8113 was a pioneer laboratory in the use of molecular modelling enabling access to the three-dimensional structure of biological objects (DNA and proteins). From this point of view, the laboratory has participated in the development of the Amber force field. The laboratory was also among the first to integrate molecular dynamics enabling the evolution of the structures to be studied.

The *in silico* models will thus be important tools for predicting the potential anti-tumour effects of the AB Science PKIs under development.

The computer models, once finalised, will make it possible to select, from among the thousands of molecules of the AB Science PKI library, a new PKI having both a specificity and a high level of efficacy, thus aiming at minimal toxic effects.

Lastly, Genomic Vision and Skuld-Tech, specialised in the development of new technologies in genomic engineering, will use biological samples taken during the clinical phases conducted by AB Science. Predictive companion tests, based on biomarkers (respectively detecting genomic rearrangements and modifications to transcriptional profiles) will make it possible to predict the response or non-response to the treatment and the toxic effects associated to the treatment in the patients treated.

About protein kinase inhibitors

Protein kinases (PK) correspond to a large family of proteins (~seven hundred proteins) conserved during evolution of the species, which thus demonstrates their functional importance in the physiology of a cell. Their principal function consists of adding phosphate ions to other proteins. This phosphorylation entails modifications to the activity of the enzyme proteins in the cell and leads to activation of the phosphate protein which engenders many cell functions such as proliferation, survival, differentiation, migration and activation. This chemical reaction requires ATP (energy source for the cell) which interacts specifically with the protein kinases via a specific binding site called the ATP pocket.

The discovery of oncogenes, and then the deregulated the nature of their activity in some tumours, as observed with PKs, changed the nature and the objectives of the projects for development of certain anti-cancer drugs. Indeed, since the activity of the molecular target of these drugs differs in normal and cancerous cells, it became conceivable to identify powerful and selective inhibitors of this enzyme activity: protein kinase inhibitors (PKIs). PKIs are almost all small chemical molecules which mimic ATP without contributing the energy necessary to the reaction. This interaction between kinase and inhibitor leads to the inactivation of this enzyme, the cessation of any signalling which could lead to cell death, and the cessation of proliferation or migration (for example in the process of formation of metastases).

During the last ten years significant advances have been made in identifying pharmacological targets and creating new active PKI molecules. These advances have been possible thanks among other things to the growth of genomics and the structural proteomics, to molecular modelling, to the elucidation of the main signalling paths, to combinatory chemistry linked to molecular optimisation techniques and to high speed screening techniques. The implementation of these techniques results in obtaining more specific and more active molecules in major pathologies, notably cancers and infectious diseases. Nevertheless, after a few years of experiments, it appears that this type of treatment very often induces the onset of acquired resistances. Moreover, in spite of the "targeted" concept of this type of therapy, these treatments induce toxic side effects such as cardiotoxicity or neurotoxicity. These toxicities are the result either of the inhibition itself of the function of the protein of interest, or an "off target" effect on an unidentified kinase.

The detailed understanding of the roles played by all of these molecules in cancers and in the acquisition of the mechanisms of resistance is crucial for the development of therapies better adapted to the needs of each patient.

About Molecular Combing
Molecular Combing is a process devised by Dr Aaron Bensimon. It consists of fixing the ends of DNA molecules in solution onto a glass surface, then uniformly stretching the molecules by retracting the meniscus (air/water interface). Long strands of DNA are thus aligned and fixed irreversibly over the whole surface. The use of fluorescent probes then enables direct viewing on each combed DNA molecule of rearrangements which can be undetectable by other technologies (deletions, duplications, inversions, etc.). The technology is thus capable of exploring the whole genome at high resolution (1kb) in one simple analysis.

About OSEO's "Industrial Strategic Innovation" Programme
The "Industrial Strategic Innovation" programme (ISI) encourages the emergence of European champions. It supports ambitious collaborative innovative projects with an industrial purpose, run by companies of a medium size (fewer than 5,000 employees) and SMEs (fewer than 250), all innovative. These projects are highly promising in the event of success: they aim to market the products of breakthrough technologies and could not succeed without public support. The aid is generally of an amount between 3 and 10 million euros in the form of repayable advances and subsidies.

About AB Science
Founded in 2001, AB Science is a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), a new class of targeted molecules whose action is to modify signalling pathways within cells. Through these PKIs, the Company targets diseases with high unmet medical needs (cancer, inflammatory diseases and central nervous system diseases), in both human and veterinary medicines. Thanks to its extensive research and development capabilities, AB Science has its own portfolio of molecules. Masitinib, a lead compound, has already been registered in veterinary medicine in Europe and is pursuing three on-going phases 3 in human medicine in pancreatic cancer, GIST and mastocytosis.

AB Science is listed on NYSE Euronext Paris (Compartment B) - ISIN: FR0010557264 – Ticker: AB
Further information is available on AB Science's website: www.ab-science.com

About Bull
Bull is an information technology company. Our mission is to be the preferred partner of our clients, corporate and administration, by optimising the architecture of their Information System, operating it and making it profitable, to support their activity and the critical processes linked to their business line.
Bull is a specialist in open and secured systems, the only European company on one of the principal links of the IT value chain.
In the field of Extreme Computing, Bull designs and develops solutions used by many research and industrial laboratories. In the United States in 2009, the Bullx supercomputer developed by Bull was voted the best supercomputer in the world by HPCwire, the biggest professional magazine in the field. In June 2010, Bull announced the most powerful supercomputer in Europe and n° 3 in the world.

For further information visit: www.bull.fr and www.bull.fr/extremecomputing
Bull press relations: Barbara Coumaros - Tel: 06 85 52 84 84 - barbara.coumaros@bull.net

About Genomic Vision SA

Genomic Vision develops molecular diagnostic tests to meet unmet needs in the fields of genetic diseases and oncology. The company exploits a proprietary technology, Molecular Combing, which enables direct viewing of genomic rearrangements in single molecules of DNA. The devising of companion tests to stratify populations of patients or monitor the efficacy of the treatments, in collaboration with the pharmaceutical laboratories, is a major area of development of the company.

Genomic Vision markets its tests directly to leading diagnostic laboratories and disseminates to the academic market a range of tools to implement the Molecular Combing technology for research purposes in the fields of cytogenetics, oncogenetics and DNA replication.

Based in Paris, Genomic Vision has raised €10m since its creation in 2004.

For further information visit: http://www.genomicvision.com

About Skuld-Tech

Skuld-tech is a biotechnology company specialised in the discovery and exploitation of biological markers (or biomarkers) characteristic of a disease or a determined physiopathological situation. The company exploits its patents and its technological know-how in the form of provision of services and in the form of products: diagnostic tools such as “companion” tests or tests making it possible to stratify or segment patients according to “typical profiles”. Skuld-tech is thus positioned in the field of “personalised” medicine which takes account of everyone’s biological or physiological differences in order to administer the most effective treatments, since they are adapted to the profile of each patient.

Further information can be found about the company at the website: www.skuldtech.com

AB Science - Financial Communication & Press Relations

Citigate Dewe Rogerson

Citigate Dewe Rogerson contacts:
Agnès Villeret - Tel: +33 1 53 32 78 95 - agnes.villeret@citigate.fr