

BIOMÉRIEUX

SILLIKER

SHANTHA

TRANSGENE

ABL

MÉRIEUX ALLIANCE

Challenging Biology Improving Health

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NEWSLETTER



Editorial

Alain Mérieux

Interview

Christian Bréchet

ADNA

ADNA receives EC approval

bioMérieux

A major stride for theranostics

Silliker

Significantly better results in 2008

Shantha

First success for the SHAN5
new pediatric vaccine

Transgene

Towards a new partnership in oncology

ABL

Diversification of research
activities and services

SynerJ

Potential savings of nearly
20 million dollars...

Fondation Mérieux

Tribute to Youssouf Issabré

A medical vision

The international public-health community is faced with three major challenges: the emergence of new pathogens, personalized medicine and food safety.

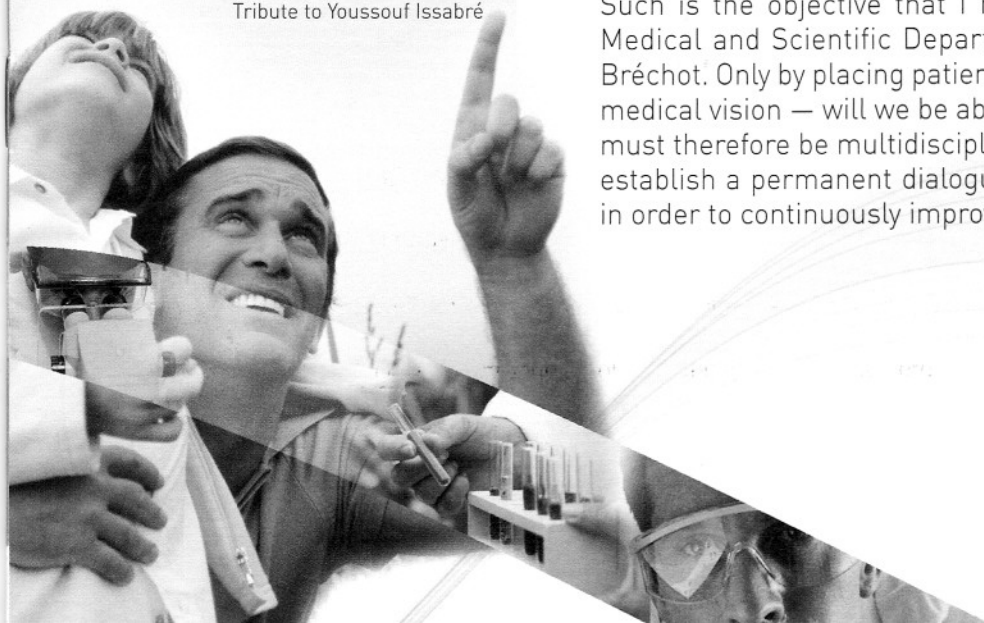
The companies that make up Mérieux Alliance possess the potential to provide solutions to these new challenges. Our experience in handling infectious diseases is extensive; our mastery of diagnostics and immunotherapy provides us with the wherewithal to make advances in personalized medicine; we are developing a comprehensive offer to prevent contamination risks in food-processing and industrial environments.

Our positions are strengthened by recent events in our companies: bioMérieux's acquisition of AviaraDx, a theranostics company specialized in oncology, the highly encouraging results of Transgene's therapeutic vaccine against lung cancer, and the EU's approval of the ADNA program.

Although we currently possess significant advantages, we must strengthen our capacity for innovation even more. For it is this capacity that determines our long-term sustainability. The extreme complexity of the medical, scientific and technological issues we are facing calls for adopting new approaches and asking some important questions.

Such is the objective that I have given to Mérieux Alliance's new Medical and Scientific Department, headed by Professor Christian Bréchet. Only by placing patients at the heart of our research — a true medical vision — will we be able to achieve it. Our innovation strategy must therefore be multidisciplinary, be founded on partnerships, and establish a permanent dialogue between researchers and clinicians in order to continuously improve the quality of patient care.

Alain Mérieux





INTERVIEW: CHRISTIAN BRECHOT

PATIENTS ARE AT THE HEART OF OUR

➔ **What are your objectives as Vice President of Medical and Scientific Affairs at Mérieux Alliance?**

Our objective is first to build, in collaboration with each company and based on thoughts and ideas that have been expressed, a true medical, scientific and technological vision within Mérieux Alliance and its entities to help them to define their medium and long-term strategies.

Secondly, it is to stimulate and strengthen innovation by bringing new concepts to the group through the creation of a network of high-level investigators and the establishment of partnerships with universities and research centers.

Overall, I would like our strategy to be focused not on businesses, but on people, on taking risks, and on strengthening synergies within and among our companies.

➔ **How can major medical and scientific challenges be anticipated and met?**

We are setting up groups of experts precisely to help us to better tackle current and future scientific challenges. They will combine their vision of clinical research and public health with data from fundamental and technological research. Their efforts will be part of what is referred to as 'translational' research, which brings together researchers and clinicians who can translate scientific findings from fundamental research into clinical practice for the benefit of patients. We want to place patients at the heart of our research.

This year these experts have already started analyzing the future of oncology biomarkers (particularly from a theranostics standpoint) and have begun discussing the future of infectious diseases as well as viral hepatitis and liver fibrosis. In 2009 other groups will focus on the evaluating the host response to pathogens and cancer in order to develop biomarkers. They will also analyze public health policies as well as the organization of care and its impact on diagnostics and vaccinology. Lastly, other groups will specifically address cancer, cardiovascular diseases and strokes.

➔ **How do you intend to promote innovation within Mérieux Alliance?**

Let me be clear: the companies in the Mérieux Alliance are already innovative! Innovation comes from ideas generated through fundamental research and the people in the medical and public health community, from questions raised internally, from all stages of R&D and support, and from needs expressed by patients and our customers.

We want to strengthen innovation within the group by developing a real 'continuum' between this activity and R&D in each company. Our goal is to be proactive, that is, to search for solutions in the academic community in a manner that is complementary to the strategic activities already in place. To do this, we intend to identify concepts and technologies that can be transferred from academic or private research laboratories to the R&D activities in our companies. Our strategy will be based on calls for research projects aimed at topics with very high potential — known as Merieux Research Grants — are aligned with the group's strategic goals. Our strategy must be built on a foundation of talent!

A HOW-TO GUIDE TO RESEARCH GRANTS

These research grants are designed to promote and identify innovative projects. They will provide investigators (junior, senior, in the medical or scientific community) in public and private laboratories with the funding needed to conduct projects on infectious diseases, cancer and cardiovascular diseases, and food and water safety. All applications will go through a rigorous review process. Those that are selected will be awarded a two-year grant, with Mérieux Alliance having the option of establishing strategic partnerships in the event of success.

There will be two types of grants:

- **Advanced Research Grants** for the most innovative projects having significant strategic advantages,
- **Starting Research Grants** for projects that, although interesting, must clearly demonstrate their feasibility.

Equivalent grants may be established in-house to support innovative projects that, despite no longer fitting in with the current strategy of our companies, nevertheless deserve to be funded and perhaps 'outsourced'.



➔ **In what areas could the group's synergies be allowed to flow?**

We must strengthen the synergies within the group so that Mérieux Alliance can make the most of its tremendous potential in *in vitro* diagnostics, vaccines (preventive and therapeutic), immunotherapy and the prevention of contamination by food and waterborne pathogens.

Cross-disciplinary programs have been created in various fields, such as tuberculosis.

We are also setting up 'structuring' actions aimed at strengthening the expertise of Mérieux Alliance and its companies in fields of common interest: scientific watch and data mining, identification of key opinion leaders, bioinformatics, and access to tissue banks and sample collections.

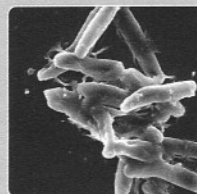
➔ **Your goals are ambitious. What resources do you have to achieve them?**

I am aware that this plan is very ambitious. Let me be clear: it is a five-year plan. We are a small team, and intend to remain one. Doctor Christine M'Rini has recently joined us as Scientific Director to coordinate all medical and scientific activities at Mérieux Alliance and to strengthen our efforts in Europe and internationally. Our team, which is based in rue Bourgelat in Lyon, is currently made up of five permanent members and around ten consultants.

Being a small team has its advantages. It allows us to remain flexible and responsive and requires us to work in collaboration with the teams in the other companies.

We are not here to create a new structure that is out of touch with the rest. Quite the contrary: we are going to work very closely with experts and consultants chosen according to the area of focus. Networking is one of our operating principles.

Furthermore, Mérieux Alliance intends to achieve its ambitions by creating, in partnership with outside investors, an investment fund for innovation and its management.



Tuberculosis: an exemplary group approach

Coordinated by Geneviève Inchauspé and Philippe Archinard (Transgene), in collaboration with Peter Kaspar (bioMérieux), this program brings together three complementary approaches: vaccines, diagnostics and public health.

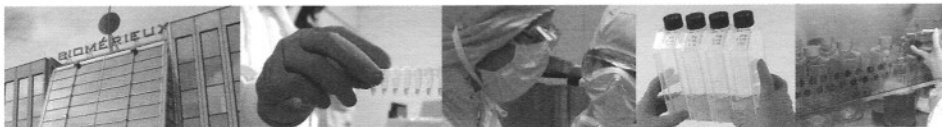
■ **Transgene** is going to draw on the expertise of **ABL** and **Shantha** to work on new vaccine strategies based on the use of MVA vectors and a prime-boost strategy.

■ **bioMérieux** is going to develop new tests to improve diagnostics for tuberculosis, which remain difficult particularly on account of the emergence of multiresistant bacterial strains. The partnership recently established with FIND fits with this goal.

■ **Fondation Mérieux** is working in the field in developing countries to conduct epidemiological studies, evaluate diagnostic practices, and new tests placed on the market.

The grants policy will enable us to identify new concepts that could guide our strategy in the future.

To tackle this pathology which poses major public-health challenges, we are going to implement a multidisciplinary program made possible by obvious synergies within the group. We are also going to call on external partners, major foundations, international organizations and other sources to fund it.



BIOMÉRIEUX



A major stride for theranostics

The acquisition of AviaraDx is undeniably the highlight of this third quarter. It marks a major milestone for bioMérieux and its long-term strategy.

Founded in 1996 in San Diego, California, AviaraDx is specialized in molecular biology and has 19 employees. Essentially focused on R&D, it develops diagnostic tests that are used in the molecular classification of cancers and to assist oncologists in making the best therapeutic decisions. It operates its own service laboratory. AviaraDx currently markets two innovative theranostics products. One allows the classification of metastatic cancers of uncertain or unknown primary origin (by determining the organs in which a cancer has started), the other allows clinicians to assess prognosis in breast-cancer patients and determine how they will respond to chemotherapy or hormone therapy.

Nearly two years ago bioMérieux decided to focus its strategy on infectious disease diagnostics and high medical-value tests. For the latter, theranostics and particularly oncology are critical elements. The theranostics partnerships with Ipsen and Merck & Co. have allowed bioMérieux to make the first advances in contributing to achieving medicine that is more predictive and personalized.

The acquisition of AviaraDx is a decisive milestone.

It strengthens bioMérieux's oncology capabilities by providing it with the means to enter the field of tissue assays, a first for the company. Their uses are particularly important in theranostics. With this in mind, it was only natural that AviaraDx be renamed bioTheragnostics.

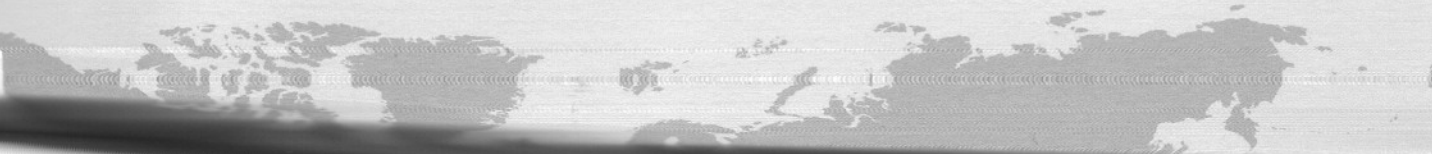
As the activities of AviaraDx and ADNA share common objectives and obvious complementarities (particularly regarding blood tests in the case of ADNA and tissue assays in the case of AviaraDx), studies will be conducted to analyze and develop the best possible synergies.

bioTheragnostics is vital to the direction bioMérieux is taking and which will allow it to shift from a strategy centered on analysis laboratories to one focused on patients and that promotes direct contact with physicians.

Lastly, although infectious diseases remain bioMérieux's core business, high medical-value tests and the potential sales of AviaraDx's products will be major engines for growth in the coming years. They will play a decisive role in the company's sustainability over the long term.

INTERNATIONAL NETWORK: FOUR NEW SUBSIDIARIES IN UNDER A YEAR

Following the official inauguration in November of a new subsidiary in Algiers by Alain Mérieux and the opening of a subsidiary in Dubai, bioMérieux now has 39 subsidiaries around the world. Since December 2007, four new subsidiaries have been opened in South Africa, Singapore, Algeria and the United Arab Emirates. They illustrate bioMérieux's continuation of its international growth strategy.





SILLIKER

Significantly better results in 2008

With revenues of USD 265 million, up 7.2% (at constant currencies and at comparable perimeter), Silliker closed the 2008* financial year with a good dynamic of growth. This growth is accompanied by a significant enhancement of its profitability, which is increasing twofold outside France. As a result, Silliker also saw its debt reduce. The Safari 2012 project initiated in March 2007 is starting to pay off despite the weak dollar.

The favorable results in the USA and Asia, which are experiencing double-digit growth, and the return to profitability of Italy and Australia also deserve mentioning.



Johannes Burlin has joined Silliker as President of Silliker North America. He will report to Philippe Sans. **Thomas VanCott**, until recently Executive VP, Operations of

ABL, replaces Johannes as CEO of ABL. Johannes will replace Georges Hibon as Chairman of ABL.

Georges will remain on the company's Board of Directors.



SUCCESS STORIES

...China: Silliker won a bid for a highly-coveted project for the Olympic Games in Beijing.

ARAMARK, the catering service provider for the athletes during the games, chose Silliker to set up a quality assurance system to ensure the safety of the food served.

...USA: Silliker just signed an agreement with WAL-MART, the world's largest retailer, to conduct sensory analyses on its house brands.

Although France had to proceed with a necessary restructuring, it was able to continue its investment policy by changing its information systems and embarking on a project to build a new chemistry laboratory in Merville, France. When the laboratory is completed, all French operations will be centralized at the Merville site.

Silliker's accelerating growth makes strengthening the group's integration all the more crucial. To achieve this, the One Silliker Company project has set three priorities:

- Harmonize information systems by standardizing hardware, software and procedures,
- Implement a corporate Quality policy,
- Develop a group-wide human resources policy.

Silliker continues its international development through two acquisitions:

- Portugal: EGL is now Silliker Portugal, the group's 15th subsidiary
- Brazil: Silliker has acquired BioAgri, one of the largest chemical analysis laboratories in Latin America. This acquisition enables Silliker to gain a foothold in South America as well as new skills in fields of the environment and agrochemicals.

More broadly, Silliker intends to confirm its presence in India, China and other emerging countries with substantial food safety requirements.

Chemistry: a strategic priority

Chemistry stands out as a key factor for growth in Silliker's medium-term strategy. The group has given itself five years to become an international leader in this expanding market. It aims to do so by focusing in particular on nutrition and instrumental chemical analysis. The goal is to work with food industry companies in analyzing the chemical and nutritional properties of products under development.

This ambitious strategy entails strengthening scientific leadership, investing in R&D, and making new acquisitions in order to expand the group's expertise.

* Financial year ended September 30, 2008.



SHANTHA BIOTECHNICS

A first success for Shan5, the new pentavalent pediatric vaccine

The new Shan5 vaccine – which had received prequalification from the WHO – received a major contract from UNICEF. This pentavalent pediatric vaccine immunizes infants from diphtheria, tetanus, pertussis, hepatitis B, and *haemophilus influenzae type b*. It meets major public health needs in the developing world. The first shipments were sent out in October.



Dr. Yaqoob Ali (COO), Mr. S Sudhakar Rao (Manager), Mr. S.V. Kotbagi (Sr.VP) and Mr. N. Rajasekar (CFO) during the packing of the first shipments of vaccine

Shantha continues its strategy of focusing on vaccines. Two products that play a key role in public health have crossed major steps in terms of Research and Development.

The **rotavirus vaccine** developed under the leadership of Raman Rao and in cooperation with the international organization PATH will undergo Phase I clinical trials in January 2009. Each year rotavirus gastroenteritis kills over 500,000 children under the age of five, primarily in developing countries.



TRANSGENE

Towards a new partnership in oncology

On September 15th, Transgene presented promising results from a Phase IIb clinical trial conducted on its therapeutic vaccine TG4010 for advanced non-small cell lung cancer. It presented these results at the annual meeting of the European Society for Medical Oncology (ESMO) in Stockholm.

The Phase IIb trial, which involved 148 patients in France, Poland and Hungary, was conducted to evaluate the vaccine's efficacy when used as an adjunct to standard chemotherapy compared to the chemotherapy regimen alone. A first paper presented at the annual meeting of the American Society of Clinical Oncology (ASCO) in June 2008 and the results of September confirm a significant benefit for patients and validate Transgene's technological platform of immunotherapeutic products.

They highlight all the benefits of the study's findings on the biological markers and demonstrate that translational research is now essential to the development of innovative products.

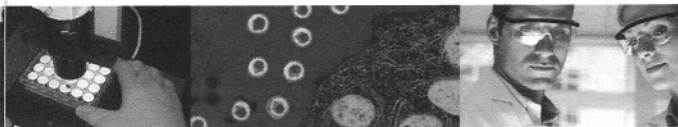
Although additional clinical results will be collected over the coming months, Transgene is already working on establishing a partnership with the pharmaceutical industry to ensure the Phase III clinical development of TG4010 for not only this form of lung cancer, but for other forms as well or at other stages of the disease.



These encouraging results come on the heels of Transgene's signing, in 2007, of a partnership agreement with Roche to continue the clinical development and marketing of its therapeutic vaccine for precancerous cervical lesions.

Transgene has marked a new step in its growth strategy and reached the objectives it set in 2005: prove the efficacy of its refocused product portfolio and establish partnership agreements with the pharmaceutical industry. Now the company intends to expand its technological platform, have one new product placed under clinical trial each year, and thus become a leader in immunotherapy treatments for cancer and infectious diseases.

The **cholera vaccine** is also undergoing Phase III clinical trials. 120,000 patients have been enrolled in the Kolkata area and the trials are scheduled to end in 2009. Although cholera (which causes acute diarrhea) is not a problem in countries with modern sanitation systems, it remains a threat in nearly all developing countries. The number of cases reported to the WHO in 2006 grew considerably, reaching figures not seen since the end of the 1990s. It is estimated that cholera causes 100,000 deaths each year, primarily in Asia and Africa.



ABL

Diversification of research activities and services

Until recently highly focused on research contracts in the field of HIV for the NIH (National Institutes of Health), ABL is now diversifying its R&D activities and the services it offers to its clients:

- Its programs address vaccines for HIV as well as microbicides, with particular emphasis on the development of *in vitro* research assays and small animal preclinical studies.
- ABL is extending its research to other infectious diseases than HIV, through new programs that focus on the infectious agents behind major international public health problems, including influenza, SARS, *Streptococcus Mutans*, *Candida Albicans*, and norovirus.
- By diversifying its activities, ABL is able to provide services not only to the NIH, but also to other North American branches of government (such as the US Department of Defense), biotechnology companies, pharmaceutical companies and other new clients.

In 2008, ABL entered into new agreements with the NIH to evaluate microbicides, develop a candidate vaccine against *Candida Albicans* and manufacture a *Streptococcus Mutans* vaccine at its GMP production facility. It has also signed an agreement with the US Department of Defense to manufacture an HIV vaccine candidate to be used in Phase I and II clinical trials in the USA and Africa.

ABL is also continuing to collaborate scientifically with the Mérieux Alliance companies to identify new vaccine targets primarily in the fields of tuberculosis (see page 3 feature), noroviruses and pneumococci.

To bolster its growth strategy, ABL is strengthening its human resources and research infrastructure by bringing in new specialists, upgrading two new laboratories to class 10,000 cleanrooms for BSL2 (BioSafety Level 2) work, and expanding its capabilities in preclinical testing on small animals.

Shantha Biotechnics has recently reinforced its management team in India by bringing in Yaqoob Ali as Chief Operating Officer in charge of manufacturing, quality assurance and control and R&D. Holding a degree from the prestigious Indian Institute of Technology of Kanpur, Yaqoob Ali brings with him extensive experience in the pharmaceutical industry. He will report to Doctor Varaprasad Reddy.