

The Pharma success rate drop in R&D is not a fatality.

Paris, France – June 12, 2013.

Recently, multiple press articles have appeared, heralding the European drive towards the implementation of "Systems Medicine", a novel approach to public health aiming to generate better, personalized treatments at lower costs. <u>On March 5, 2013</u>, appeared the announcement that "Bio-Modeling Systems is recognized for the second time as a major contributor to Systems Medicine by the European Commission's DG Research".

Psychiatric and nervous systems diseases are prominent amongst the major public health issues to be addressed by "Systems Medicine". Indeed, mental disorders are the main contributors to the global financial burden of non-transmissible diseases, well head of cardiovascular diseases and cancer. Yet, they remain misunderstood, under-estimated and treatments are unsatisfactory. On May 2, 2013, it was announced that "Bio-Modeling Systems discloses the first scientific results of its European research program on chronic anxiety mechanisms (DECIUS™) at the 9th International Workshop on Computational Neuropsychiatry in Munich". On April 2, 2013 appeared the announcement that "BMSystems & the FondaMental Foundation join forces to decipher the immuno-inflammatory mechanisms that could give rise to psychiatric diseases and open novel therapeutic avenues", followed, on June 13-16, 2013 by Pr. Leboyer's Keynote Speech, at the 10th International Conference on Bipolar disorders in Florida, disclosing the first results of the FondaMental Foundation and Bio-Modeling Systems R&D collaboration in CNS diseases.

However, broad implementation of "Systems Medicine" will require novel, disruptive conceptual frameworks leading to innovative information technologies (IT) and bio-informatics tools. <u>On March 22, 2013</u>, it was announced that "BM-Systems (Paris) and Persistent Systems (India) have launched a strategic joint initiative in Systems Biology through a R&D program to accelerate Mechanism-Based Drug Discovery and help eliminate the use of animals in contact allergy testing". <u>On June 26, 2013</u>, BM-Systems' CSO (Dr. François Iris) is invited at the <u>Teratec international forum</u> (High performance Computing) to present our approaches to effective "Systems Medicine".

Few R&D entities can exhibit such a track record addressing "Systems Medicine", embodied by on-going programs and filed patents:

- IDUNN: Successfully completed research program that led to a novel combinatorial treatment addressing age-related degenerative disorders, such as Parkinson's disease; Patent pending.
- WO/2010/02913-1. Combinatorial treatment for psychiatric disorders; Patent ownership shared with the CEA and exclusively licensed to a start-up created at the CEA in 2013.
- DECIUS: On-going self-funded European collaborative research program addressing the identification of biomarkers attached to chronic anxiety.
- PSY-LICO: On-going research program with the FondaMental Foundation to decipher the immunoinflammatory mechanisms that could give rise to psychiatric diseases, such as bipolar disorders and schizophrenia, and thus open novel therapeutic strategies
- FIBROMYLAGIA. Identification of the mechanisms leading to the disease; program initiated.

BM-Systems' successes may have something to do with our long held tenet that "it is time to think differently and stop searching under the street light".

What we can do for ourselves we can perhaps also do for you. Could it be worth considering?

About Bio-Modeling Systems (BMSystems):

Bio-Modeling Systems, an innovative company founded in 2004, is the first and, to date, only company to successfully create in-silico heuristic models validated in-vivo. BMSystems' heuristic models, built by its biologists using an integrated IT solution called CADI [™] (Computer Assisted Deductive Integration) have led to discoveries, patents, and operational businesses in the fields of infectious diseases, immunology, neurology, psychiatry, oncology, dermatology and innovative bioprocesses for industrial biotech. BMSystems' models describe the biological phenomena involved in pathological states and provide new mechanisms to explain the cause of certain diseases, identify and select predictive biomarkers, offer new combinations of molecules and new therapeutic strategies, thereby contributing to the development of Mechanism-Based Medicine.

The consequences are

- i) A significant reduction of short-term risks in therapeutic developments,
- ii) A new life for clinically well characterized molecules, and
- iii) Preservation of the medium term potential for new drugs development.

BUSINESS - VALUE PROPOSITION

- Disease understanding / (re) definition (biomedical).
- Target discovery / validation (biomedical)
- New therapeutic strategies (biomedical).
- New association / combination of existing drugs (biomedical).
- Identification / selection of pertinent predictive Biomarkers (biomedical).
- R&D programs evaluation (biomedical).
- Drug repositioning / reprofiling / rescue (biomedical).
- Proposition of new bioproduction processes through micro-organisms' modifications (biomedical, chemistry, environment, energy,...).

BMSystems markets: All applications linked to life sciences

- Pharma, diagnostic, cosmetics: Red/biomedical Biotech.
- Chemistry: White/Industrial biotech.
- Environment: Yellow/environmental Biotech.
- Energy: Renewable Energy Biotech.

CADI™ RESEARCH - PUBLICATIONS

CADI[™] Models publications in prestigious international peer-reviewed journals

- 2012: Neurodegenerative & Psychiatric disorders: Pharmacopsychiatry publishes the first review describing a productive vision of Systems Medicine that will change R&D organization and interactions between clinicians & researchers while revealing how the world's first explanation of the mechanisms of the Creutzfeldt-Jakob disease led to the discovery of a truly innovative psychiatric treatment.
- 2011: PSYCHIATRY: Publication (in Pharmacopsychiatry) with the Max Planck Institute of Psychiatry in Munich that describes a new analytical paradigm to definitively move research away from plethoric statistical biomarkers.
- 2010: INFECTIOUS DISEASES: Publication (in Biosecurity and Bioterrorism) with Pherecydes-Pharma describing the production of genetically engineered virulent phage banks in the detection and control of emergent pathogenic bacteria.
- 2009. TISSUE DIFFERENTIATION: CADI model validated in vivo (Medecine & Science [French]) explaining the hitherto obscure developmental phenomenon known as "Mullerian regression".
- 2005, CANCER: Publication in collaboration with the INSERM unit 553 (Journal of molecular Endocrinology) of the model, validated in vitro, explaining the mechanism behind therapeutic resistance to Tamoxifen in breast cancer cells.
- 2003, CANCER: World first. Publication in collaboration with the INSERM unit 553 (Nucleic Acids Research) of the first ever in-silico model of a complex human disease validated in-vitro.

Collaboration to Scientific reference books

- 2010, The European Commission "From Systems Biology to Systems Medicine" report: BMSystems' heurisitic systems biology research contribution to the report. The world's first explanation of the mechanisms of the Creutzfeldt-Jakob disease led to the discovery of a truly innovative psychiatric treatment recognized as one of the three best world's practice in systems medicine
- 2008, CNS: Biomarkers for Psychiatric Disorders. (Ref. ISBN: 978-0-387-79250-7, November 2008).Dr. Francois Iris, author of the integrative biology chapter of the Book. The editor, Christoph W. Turck, is head of the Proteomics and Biomarkers branch at the Max Planck Institute of Psychiatry and holds faculty appointments in the Department of Biochemistry at Ludwig Maximilians University Munich and the International Max Planck Research School for Molecular and Cellular Life Sciences
- 2008, CNS: Integrative Biology in the discovery of relevant biomarkers monitoring cognitive disorders pathogenesis and progression. BioTribune Springer publisher Vol. 28, august 2008.
- 2005, Systems Biology: Computer-Assisted Integration into Biological Pathways of Modulated Gene Expressions Patterns. In « Bioinformatics: New Research », Yan PV editor, Chapter IV, pp 81-100 Nova Publishers (ISBN: 1-59454-242-2 2005)

BMSystems has successfully completed programs in infectious diseases, oncology, neurology, psychiatry, dermatology, immunology and metabolic disorders which led to patents and the creation of new companies exploiting these patents.

For more information and access to presentations & publications, please visit <u>http://www.bmsystems.net</u>.

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