

MANAGEMENT SUMMARY

[\(download\)](#) the short corporate presentation for details and links to websites)

"Correct understanding of life mechanisms makes novel integrated diagnostics, therapies & preventive solutions discovery smarter, faster & cheaper for healthcare, diagnostics, health technologies, nutrition, and cosmetics!"

Bio-Modeling Systems is the world's first Mechanisms-Based medicine company that changed the discovery paradigm to create novel medical meanings from unreliable heterogeneous sources of data to generate validated & directly exploitable first in class heuristic non-mathematical mechanistic CADI™ Discovery models.

Created in 2004, profitable since 2006, thanks to our recurrent clients, our patented collaborative discoveries already led to:

1. *A world's first in neurodegenerative diseases* with CEA: 2 awards in the US & Europe.
2. *Pherecydes-Pharma: BMSystems' spin-off, MR infections therapies*, publication, world's first clinical trial with phages in Phase I/II,
3. *Theranexus: CEA Life Sciences' spin-off exploiting CEA/BMSystems' copatent* WO/2010/029131, in CNS therapies, successful Phase I, Phase II entry.

With CADI™ Discovery, BMSystems *possesses a truly unique competitive advantage*: the ability to address and exploit the two major issues in life sciences

1. the *enormous complexity of life's mechanisms*, and
2. the *significant* and *growing unreliability* of scientific and clinical publications.

Through its dual contractual & collaborative business model, BMSystems

1. *proposes robust R&D and Business decision-making support*, and
2. *discovers cost-effective, lower risk, patentable novel integrated solutions*, for medicine, health technologies, nutrition and cosmetics

1-BMSystems Group at a glance

- *Independent Private Company* incorporated in 2004. 100% owned by its founders.
- *Profitable since 2006*, thanks to our recurrent clients.
- We only sell the results of the R&D programs, not our proprietary technologies.
- 100% biology driven company focused on discovery
- Proprietary CADI™ Knowledge Database of mechanisms & interactions.
- *Not domain-dependent*, but information-dependent.
- Markets: Pharma, Cosmetics, Nutrition, Health Technologies, Connected health,
- highly productive 24 FTE* of which 9 FTE on CADI™ Discovery programs only.
- Strong & long term strategic R&D collaborations (>100 people collaborating).
- *Dual business model*: Contractual and/or Collaborative R&D programs.
- Outstanding internal pipeline of programs ready for collaborations.
- *2 therapeutic spin-offs at the clinical stage, 4 issued patents, 10 publications.*

Potential competitors: Key Opinion Leaders, dominant thinking companies or pharma Systems Biology or bioinformatics teams argue they can do the same. We are always open for discussions & comparisons on success rates and outputs for patients.

2-An experienced multidisciplinary founders' team



Dr. François Iris (PhD), Chairman, CSO-CTO - Heuristic modeling specialist French-New-Zealander. Geneticist, physiologist & molecular biologist. **40 years of experience in life sciences in academia and industry** : Dept. of Medicine University of Otago, The Christchurch School of Medicine (NZ) Millennium Pharmaceuticals' (USA) collaborator of Nobel Laureate Prof. Jean Dausset. Inventor of CADITM and of new technologies in molecular biology. MRC Overseas fellow, Member of H.U.G.O., Wellcome Trust; etc..



Manuel Gea, C.E.O & VP R&D I. S. – Operational Research & business develop. specialist 30 years of experience in IT and life sciences. Scientific Engineering Degree from Ecole Centrale Paris. Various experiences R&D and business from consumer goods Industry to cosmetics, biotechnology & pharmaceutical companies: Colgate-Palmolive McKinsey, Boehringer Ingelheim, HemispherX Biopharma, Pherecydes-Pharma, BMSystems; etc..



Gérard Dine (MD, PhD), Chief Medical Officer - Physician, biologist 35 years of experience in clinical and medical research. Head of hospital's Hematology Dept. Former President of the Institute for Sports Medicine; IRMES - Institute for Research in bioMedecine and Epidemiology of Sport, etc..



Paul-Henri Lampe, CIO & Systems Integration Director - Systems Integration specialist French-American. 20 years of experience in Systems integration in healthcare. Scientific Engineering Degree Ecole Centrale Paris. Former IBM Systems Integration Manager. Former Information Systems Manager, Hospital in Paris.

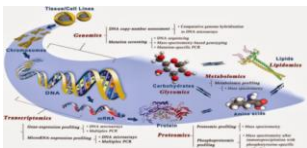


Pablo Santamaria, IT & Internet Systems Director - Internet technologies specialist 30 years of experience in Internet technologies and life sciences. Scientific Engineering Degree from Ecole Centrale Paris, Founder and President of the computing firm Formitel, Glaxo Pharma (Evreux, France)

3-Why did we need to change the discovery paradigm?



1-The industry is under high pressure by too high failure rates and payers no more willing to pay premium therapies with very limited patient benefit.



2-The limits of the big Pharma model. Decades of investments in Omics technologies and Systems Biology programs produced few relevant results due to 3 "side effects" and a conceptual mistake: Life mechanisms are complex not complicated!



3-The "mirage" of Artificial Intelligence (AI) that MUST follow rules in a world where humans massively do not! Currently the "Garbage in garbage out" reality is not correctly treated by digital giants who consider life as only complicated.



4-The unreliability of scientific and clinical publications is increasing. "Many published research findings are false or exaggerated; an estimated 85% of research resources are wasted." (Stanford University), and the valuable negative results are not published.

4-The Mechanisms-Based Medicine Concept:

Understanding and validating the mechanisms of a disease/disorder becomes the first objective.

Finding the most adapted solutions is a necessary consequence of the first objective.

1. **DISEASE/DISORDER:** Describe the physiopathology of the disease/disorder with clinicians and patients feedback.
2. **MECHANISMS:** Discover the causal versus symptomatic mechanisms of the disease/disorder.
3. **BIOMARKERS:** Indirectly based on causal mechanisms, identify relevant biomarkers or specific combination, signatures of biomarkers (biological, imagery, physical signals, etc...) that could measure defined mechanistic deregulations at different stages of the disease/disorder.
4. **TARGETS:** based on the causal mechanisms, identify what could be the best targets (not only one) to specifically address the causative deregulations.
5. **SOLUTIONS:** We harness the mechanisms. Propose the most practical solutions to address the relevant mechanistic deregulations. It is important to notice that the proposed solutions, integrating diagnostics, therapies & patients follow-up, can be combinations of existing drugs, nutriments, devices, e-health, disease prevention tools and services, etc.
6. **FEEDBACK LOOP:** Integrate the results from e-R&D or e-Health experimentations into the validation process to improve global patient and disease/disorder follow-up.

5-The 5 CADI™ Discovery Principles

1. Mechanisms-Based Medicine
2. Architectural Principle
3. Negative Selection Principle
4. 4 Steps Validation Principle
5. Integrated Solutions Principle

6-CADI™ Proprietary Technologies and Know-how:

Industrial secrets to protect the CADI™ platform:

- CADI™ Search (data acquisition & mining),
- CADI™ Framework (data organization & structuring),
- CADI™ Fiber-N (integrative engine),
- CADI™ View (model representation & visualization),
- CADI™ knowledge Database.

Patents produced during the collaborative research programs for spin-offs or out-licensing:

- TAPE Patent: WO/2008/093010- December 2006,
- AB-ACCUS patent: WO/2008/093009 - December 2006,
- RIPH patent: PCT/FR2010/050796 – May 2009,
- CNS patent: WO/2010/029131 - September, 2008 (psychiatric disorders)

7-BMSystems' internal and collaborative R&D programs

Not domain dependent, we already conducted R&D programs in the fields of neurology, inflammation, metabolism, immunology, addressing neurodegenerative diseases (Creutzfeldt-Jakob's, Parkinson's & Alzheimer's diseases), psychiatry, autism, cancer, diabetes, longevity/aging, infections, dermatology, skincare and cosmetics.(see map below)

Program Name	Validation / Business Partner(s)	CADJ™ compliance	CADJ™ vers. 0	Ind. Valid.	Patents / Publi.	First Proof of Concept (POC)	Mid scale or preclinic. P.O.C.	Business launched
Nano-Bioagents	Pherecydes							Phase I/II
TAPE (protein improvement)	Pherecydes							Completed
Chronic Fatigue Syndrome	Open							
Ebola virus ecology	Open							
Hepatitis C	Open							
Auto-immune global concept	Open	high Interest						
Psychiatric combination treatment	CEA Life Sciences							Phase II entry
Creutzfeldt-Jakob disease mechanisms	CEA Life Sciences						Completed	
Alzheimer Disease Mechanisms	Open		high Interest					
Parkinson's Disease Therapy	Open		high Interest					
Psychiatric inflammatory mechanisms	FondaMental Foundation							
Fibromyalgia, facial pain	Aepodia							
Pain (Central/Peripheral)	Open							
Migraine Mechanisms	Open							
Multiple Sclerosis Mechanisms	Open							
Psychiatric disorders biomarkers	Max Planck Munich							
Metabolic Disorders Therapy	Open		high Interest					
Etiology & Epigenetic for metabolic disorders	IISER Pune		high Interest					
Hypercholestermia Mechanisms	Open							
New global concept for Diabetes type 1	Open							
Metabolic Syndrome	Open							
Breast cancer-Hras	INSERM					Completed	Completed	
Tamoxifen resistance	INSERM					Completed	Completed	
Specific Metastasis control	INSERM				Completed			
Encysting Tumour Therapy	Open	high Interest						
Müllerian regression Mechanisms	CNRS				Completed			
Adipocytes growth control	Open							
Skin Contact Allergy Mechanisms	Open		high Interest					
Skin pigmentation Mechanisms	Open		high Interest					
Skin aging Mechanisms	Open							
Program Synthons	ARD-IBT-L'Oreal						Completed	
Program Synthons	ARD-IBT-Rhodia			Completed				
Program Synthons	ARD-IBT-Arkema			Completed				
Human Glycosylation with Yeast	Open							

Infection-Immunology	Oncology/Inflammation
CNS-PNS/Inflammation	Tissue Differentiation
Industrial biotech/ bioprocesses	Metabolism/Inflammation
Dermatology/Inflammation	

8-The 5 BMSystems' solutions to critical & high impact issues.

1. GO-NO GO decision before product acquisition or for portfolio risk analysis.
2. GO-NO GO decision before next development phase.
3. R&D program Rescue for a program facing critical issues during its lifetime.
4. External R&D "B plan" program when the "A plan" cannot be rescued.
5. Exploratory Discovery program to generate novel causal mechanism concepts.

9-CADI™ Models published in prestigious peer-reviewed journals:

- [2014, CNS Psychiatry publication](#): American Journal of Psychiatry and Neuroscience. Second publications with the Max Planck Institute of Psychiatry in Munich: Differential proteomics analyses reveal anxiety-associated molecular and cellular mechanisms in cingulate cortex synapses. The first output of the DECIUS CNS research program.
- [2012, CNS NEURODEGENERATIVE & PSYCHIATRY](#): PharmacoPsychiatry publishes the first review describing a productive vision of Systems Medicine that will change R&D organization and interactions between clinicians & researchers & reveals 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, CNS PSYCHIATRY](#): Pharmaco Psychiatry publication: Proteome-Based Pathway Modelling of Psychiatric Disorders. Publication with The max Planck Institute of Psychiatry in Munich
- [2010, INFECTIOUS DISEASES](#): Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science :Genetically Engineered Virulent Phage Banks in the Detection and Control of Emergent Pathogenic Bacteria. Publication with Pherecydes-Pharma.
- [2009, TISSUE DIFFERENTIATION](#): Médecine & Sciences: Müllerian duct regression explanation. Integrative systems biology & experimental Biology. Publication with CNRS experimental data.
- [2005, CANCER](#): Journal of molecular Endocrinology: Integrative analysis of gene expression patterns predicts specific modulations of defined cell functions by estrogen and Tamoxifen in MCF7 breast cancer cells. Publication in collaboration with INSERM unit 553.
- [2003, CANCER](#): Nucleic Acids Research: Integrated transcriptome analysis of the cellular mechanisms associated with Ha-ras-dependent malignant transformation of the human breast epithelial MCF7 cell line. Publication in collaboration with INSERM unit 553. World first. First in-silico model of a complex human disease validated in-vitro and published.

10-Collaboration to scientific reference books:

- [2014, Dermatology Cosmetics](#). The first reference book on "Computational Biophysics of the Skin" edited by Prof. Bernard Querleux , scientific chairperson of the International Society for Biophysics and Imaging of the Skin
- [2008, CNS](#): Biomarkers for Psychiatric Disorders. (Ref. ISBN: 978-0-387-79250-7, November 2008). Dr. François Iris, is the author of the Integrative Biology chapter of the book. The editor, Prof. Christoph W. Turck, is head of the Proteomics and Biomarkers branch at the Max Planck Institute for Psychiatry

11-Useful links:

- BMSystems' [short presentation](#)
- BMSystems' [full presentation](#) **with the 10 POCs and the publications.**
- BMSystems' [scientific presentation](#).
- [The 7 critical issues](#) R&D managers should urgently address to secure their decision making process & the future of their company!
- Author's LinkedIn Posts: <https://www.linkedin.com/today/author/871235>

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