

CLEAR & BOOST CD38+ CELLS: ACT ON INFLAMMATION RESOLUTION & TISSUE HOMEOSTASIS to protect key target organs (Heart & Kidney) in the context of metabolic and age-related disorders

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THE ORGANIZATION

Spin-out from Paris Brain Institute (Pitié Salpêtrière Hospital, France). Incorporated in 2016.

<https://www.encefa.com/>

Encefa develops First-in-Class CD38 drugs (3 international patents filed) against a large range of age-related diseases. 2 ongoing programs: NC-P7 against Cardio-Metabolic Diseases and NC-B8 against neuro-degenerative diseases

THE NEED

Metabolic Cardiomyopathies, related **Heart Failure**, and **Kidney Diseases** affect respectively more than 170 million people (US & EU) and 10% of the population worldwide. Moreover, whereas the first risk factors of developing these diseases are obesity, diabetes and aging, this prevalence goes increasing with the elderly population and our lifestyle.

These diseases constitute a major unmet medical need: no treatment is available to effectively protect key organs. However, the latest scientific developments point aging, autophagy and metabolism as key pathways to be targeted for a therapeutic purpose.

EXECUTIVE COMMITTEE



Mrs. Laurence Bressac

Executive Chairman & CEO, co-founder, formerly consultant at Deloitte, development of SME



Dr Damien Toulorge

CSO, co-founder, PhD, Neuroscientist, formerly in academic and private sectors, with Pitié Salpêtrière Hospital and Pharnext



Mr Serge Guerreiro

Co-founder, Neuroscientist, drug development at Pitié Salpêtrière Hospital and Pierre Fabre.

FIRST-IN-CLASS DRUGS LEVERAGING ON AN AGE-RELATED TARGET TO BRING ENERGY & ACT ON THE DEGRADATION PATHWAY OF RELEVANT CELLS

- **Encefa** drugs bind a specific epitope on CD38 to directly activate CD38+ cells **ENERGY METABOLISM** (Glucose uptake and ATP production) and **AUTOPHAGY FLUX** (up to lysosomal exocytosis), both in an insulin and NAD-independent pathway, while boosting **NAD+ levels**.
- CD38 is an **AGE-RELATED TARGET**, known to be heavily expressed on activated immune cells (incl. M1 macrophages), and on suffering cells of key tissues and organs (incl. adipocytes, cardiomyocytes, kidney). CD38 expression is directly linked to senescence mechanisms and thereby increases with many pathological conditions and aging.

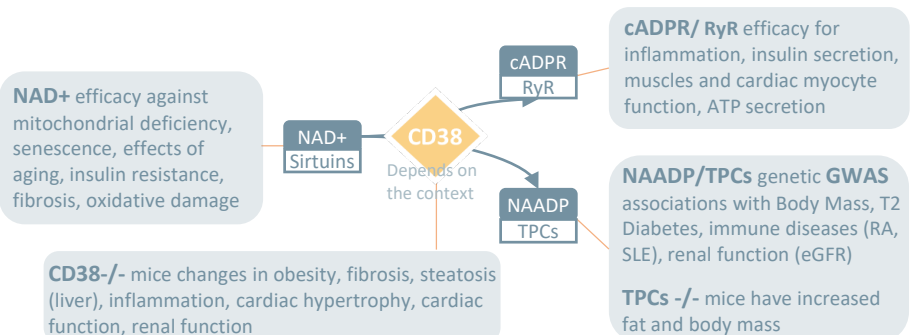


Encefa CD38 drugs are FIRST-IN-CLASS: they uniquely and specifically act on suffering and pro-inflammatory cells, to (i) restore their energy metabolism, (ii) activate their degradation pathway → to protect tissues.

CD38 AND ITS SIGNALING PATHWAYS: LINKS WITH THE METABOLIC SYNDROME AND RELATED DISEASES

ENCEFA novel CD38 therapeutic approach harnesses CD38 powerful enzymatic activity, including NAADP, cADPR and NAD+ metabolites.

Strong links with cardiometabolic diseases and their complications have been published for CD38, but also importantly for CD38 signaling pathways:



Encefa CD38 drugs uniquely modulate CD38 enzymatic activity to fully reap the benefits of both CD38 expression and its signaling pathways biological action.

NC-P7 A FIRST-IN-CLASS LEAD PRODUCT, READY FOR PRECLINICAL DEVELOPMENT

NC-P7 is **Encefa's** lead product for cardiometabolic diseases.

- NC-P7 is a **proprietary compound**, with an optimized efficacy and development properties, cross-reactive (H, C, D, R, M), to be administrated intravenously (once a month) or subcutaneously (once a week).
- NC-P7 demonstrated in vivo:
 - ✓ highly effective (human cells and in vivo),
 - ✓ good safety profile (**no immunosuppression, no hypoglycemia**),
- NC-P7 is 18 months away from IND/ IMPD filing.

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ADVISORS

CLINICAL AND PRECLINICAL DEVELOPMENT

Prof. Geneviève Derumeaux

Senescence, metabolism and cardiovascular diseases,
Mondor Institute, Paris, France

PRECLINICAL MODELS

Prof. Laurent Tiret

Ecole nationale vétérinaire d'Alfort, Paris, France

PRODUCT DEVELOPMENT

Dr. Gilles Guichard

CNRS, European Institute of Chemistry and Biology

INTELLECTUAL PROPERTY

ICOSA
European Patent & Trade Mark Attorneys

REGULATORY & CMC

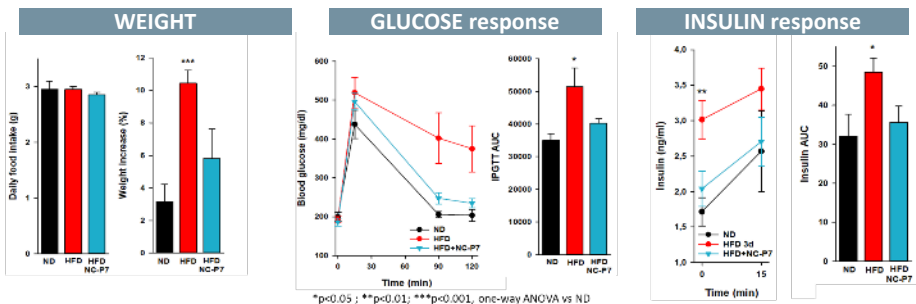
VCL
Vision Consulting Life Sciences

INTELLECTUAL PROPERTY FREEDOM TO OPERATE

Encefa fully owns its entire IP covering all CD38 compounds which activate its specific MOA for cardio-metabolic and inflammatory diseases, and from the IP protecting NC-P7 sequences. Portfolio of 3 patents recently filed.

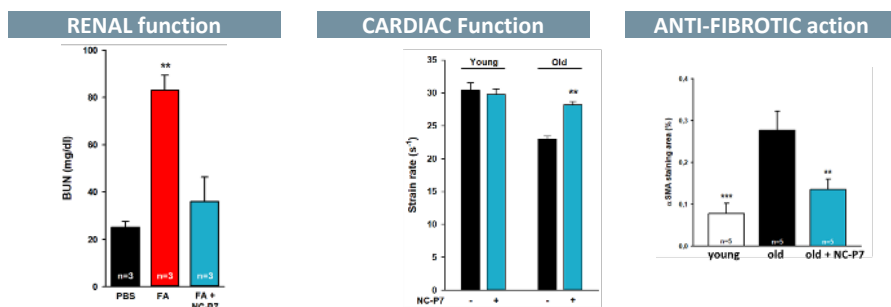
NC-P7 EFFICACY IN VIVO – selection of results

NC-P7 *in vivo* -- HFD mice model (short term HFD, 3 days):



Renal failure mice model (AKI):

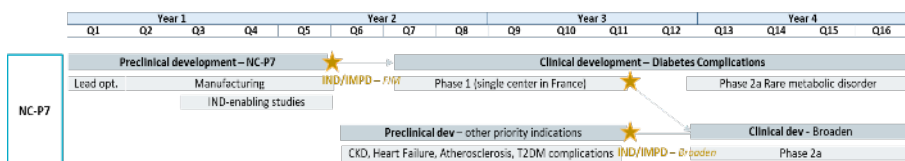
Old vs. young mice model (12 months):



Encefa NC-P7 lead candidate demonstrated:

- strong anti-diabetic properties,
- an ability to protect organs and tissues,
- an ability to modulate inflammation (inflammation resolution, no immuno-suppression),
- with a high tolerability.

NC-P7 DEVELOPMENT PLAN



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PARTNERING

NC-P7 Unique differentiating features

Therapeutic Benefits	A disruptive MOA serving an innovative ANTI-AGING approach against cardio-metabolic diseases	✓
	Strong preclinical data to be translational to human : (1) In vivo efficacy in 5 mouse models, (2) efficacy in dogs, (3) MOA validated on human cells, (4) no safety red flag, promising overall tolerability	✓
	Companion biomarkers for (1) patient inclusion, (2) dose-finding studies, (3) personalized medicine	✓
	Clear clinical strategy to accelerate approval	✓
Commercial Benefits	Breakthrough innovation: Encefa reinvents the use of CD38	✓
	Strong patent Protection: Large coverage, sequences protection, Coverage until 2040 to be extend through 2045	✓
	Unique competitive advantages	✓

• **Encefa** is looking for funding upcoming stages of preclinical and clinical development of its CD38 lead candidate product NC-B8 until first clinical trial results of efficacy (Phase 2A against diabetes complications), and IND/IMPD for other cardio-metabolic diseases.

• **Encefa** is also open for early partnering with a pharmaceutical company to co-develop NC-P7 against cardio-metabolic diseases.

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