



THE CARDIOVASCULAR DISEASES
EXPERTS

part of
JANVIER GROUP
BIOSCIENCES





OUR DNA

Your key partner in
DRUG DISCOVERY
PRECLINICAL PHARMACOLOGY
CLINICAL BIOANALYSIS
RESEARCH MODELS & SERVICES
BIOMANUFACTURING



Global leader in RESEARCH MODELS & INNOVATIVE SOLUTIONS

Proudly supporting over **3,500 clients worldwide** in achieving their objectives thanks to a **tailor-made approach**.



Empowered by EXPERTISE

Our thriving team of 735 experts includes **150 PhDs** and is solely dedicated to **driving your research to success**.



Cutting-edge INFRASTRUCTURE

Our state-of-the-art facilities set **industry benchmarks worldwide for precision, performance, and innovative power**.



INDEPENDENCE as a strength

As the last European **family-owned** company in this sector, our independence allows us to **make unparalleled quality our primary focus**.



KEY AREAS OF EXPERTISE



Oncology



Immunology



Infectious
diseases



Inflammatory
diseases



Metabolic
diseases



Cardiovascular
diseases



Auto-immune
diseases



Urogenital
diseases



Rare diseases

GROUP OFFERING

Tailor-made solutions based on gold-standard predictive models

RESEARCH MODELS & SERVICES

MODEL CREATION & BREEDING SERVICES
Contract breeding, reproductive sciences, ...

FACILITY
MANAGEMENT

LARGE RANGE OF MODELS
Immunodeficient, Humanized PBMC/CD34, Immune Checkpoint,
Liver-humanized, Preconditioned, ...

BIOLOGICAL PRODUCTS
& TISSUES

Support all the *in vitro* / *in vivo* studies

DRUG DISCOVERY

Target Id / Validation



Hit Id / Hit to Lead



Lead Optimization

SMALL MOLECULES

BIOLOGICS

CELL THERAPIES

PRECLINICAL PHARMACOLOGY

EFFICACY EVALUATION

Anti tumor drugs

Autoimmune
Inflammatory

Metabolic diseases

Cardiovascular diseases

Urogenital disorders

Liver-related disorders

IN VITRO / EX VIVO

- 40+ PDX-derived cells
- 2D/3D cell culture
- 15+ organoids
- Immuno-histochemistry
- Histology
- Flow cytometry
- Multi-omics
- Immunology assay
- Biochemistry analysis
- Molecular biology

IN VIVO

- 250+ PDX models (breast, lung, colorectal, urogenital, ...)
- 40+ syngeneic tumor models
- 40+ CDX models
- FRG® liver-humanized mice
- Imaging
- Microsurgery
- Functional pharmacology
- Short-term cytotoxicity
- Toxicology (non-GMP)
- DMPK/ADME

CLINICAL BIOANALYSIS

BIOMARKER DISCOVERY

Biobanking

Genomics & Epigenomics

Transcriptomics

Proteomics

Bioinformatics

BIOMANUFACTURING

MONOCLONAL ANTIBODIES
& RECOMBINANT PROTEINS

PLASMID DNA

CELLS

Support the drug
discovery, preclinical and
clinical phases

GROUP OFFERING

Tailor-made solutions based on gold-standard predictive models

RESEARCH MODELS & SERVICES

MODEL CREATION & BREEDING SERVICES

Contract breeding, reproductive sciences, ...

FACILITY MANAGEMENT

LARGE RANGE OF MODELS
Immunodeficient, Humanized PBMC/CD34, Immune Checkpoint,
Liver-humanized, Preconditioned, ...

BIOLOGICAL PRODUCTS & TISSUES

Support all the *in vitro* / *in vivo* studies

DRUG DISCOVERY

Target Id / Validation

Hit Id / Hit to Lead

Lead Optimization

SMALL MOLECULES

- HTS: AS-MS screening with a 2-million compounds library
- Compound libraries (exclusive/non-incl., frag./covalent)
- Organic & medicinal chemistry
- Custom synthesis, route scouting & analytical chem.

BIOLOGICS

- mAbs discovery by single cell technology (HTS)
- Generation & selection of Lead Candidates
- Engineering of mAbs & recombinant proteins
- In vitro pharmacology / in vivo pharmacology

CELL THERAPIES

- Drug candidate targeting with human primary T cells
- CAR (T/NK) & TCR design for cell therapies
- CRISPR-Cas 9, Immunomics

PRECLINICAL PHARMACOLOGY

ANTI TUMOR DRUG EFFICACY

- Prostate, breast, bladder, colorectal, lung, pancreas, ovaries, pediatric.

AUTOIMMUNE & INFLAMMATORY EFFICACY

- IgG4-Related disease, psoriasis, Peritonitis, IBD, Lupus, Prostatitis, Cystitis

METABOLIC DISEASES EFFICACY

- Obesity - Insulin resistance and diabetes, MASH, Kidney diseases, Fibrosis, Dyslipidemia, Atherosclerosis

CARDIOVASCULAR DISEASES EVALUATION

- Acute/chronic myocardial infarction, HTA, vascular diseases, cardiomyopathy, HF (reduced or pEF), sepsis, takotsubo cardiomyopathy, onco-cardiology, rare diseases, cardiac arrhythmias

UROGENITAL DISORDERS EVALUATION

- Endometriosis, urinary incontinence, overactive bladder, lithiasis, benign prostatic hyperplasia, M/F infertility, pre-term labor, polycystic ovarian syndrome, sexual dysf., acute/chronic diseases

IN VITRO / EX VIVO

- 40+ PDX-derived cells
- 2D/3D cell culture
- 15+ organoids
- Immuno-histochemistry
- Histology
- Flow cytometry
- Multi-omics on animal or human samples
- Immunology assay
- Biochemistry analysis
- Molecular biology

IN VIVO

- 250+ PDX models
- 40+ syngeneic tumor models
- 40+ CDX models
- FRG® liver-hu mice
- Imaging
- Microsurgery
- Functional pharmacology
- Short-term cytotoxicity
- Toxicology (non-GMP)
- DMPK/ADME

CLINICAL BIOANALYSIS

BIOMARKER DISCOVERY

Biobanking
Genomics & Epigenomics
Transcriptomics
Proteomics
Bioinformatics

BIOMANUFACTURING

MONOCLONAL ANTIBODIES
& RECOMBINANT PROTEINS

PLASMID DNA

CELLS

Support the drug discovery,
preclinical and clinical
phases

MEET OUR FAMILY



Antibody discovery



Small molecules
for drug discovery



Predictive models & CAR-T
preclinical solutions



Preclinical expert
in cardiovascular disorders



Preclinical expert
in metabolic disorders



Preclinical expert in oncology,
PDX, PDX-DC, CDX



Preclinical expert in urogenital
disorders, PDX, Organoids



Liver-humanized mice
& associated solutions



Biomarker discovery
& engineering



Engineering
services &
biomanufacturing



Research models
& associated solutions



WHY US



COMMITMENT TO EXCELLENCE

Our rigorous **ISO-certified quality strategies** help us consistently deliver outcomes that **exceed expectations**.



INNOVATION

Our state-of-the-art models and associated services, have been recognized for their ground-breaking impact in the scientific community.



TAILORED SOLUTIONS

We offer highly customized solutions that fit the specific needs of your research projects, based on a range of highly-specific, gold-standard models.



GLOBAL REACH WITH LOCAL EXPERTISE

Our **global presence and local teams** ensure seamless collaboration across borders, making us the ideal partner for your **international** research needs.



STRONG SCIENTIFIC SUPPORT

We offer **guidance with all our services**. Join a team of **experts**, available from start to finish to ensure the success of your projects.



CURIOSITY, CREATIVITY, PASSION

Our team's **passion and enthusiasm** drive every project we undertake. Our experts infuse **creativity and dedication** to every stage of your research.



MAXIMIZING GOVERNMENT R&D FUNDING OPPORTUNITIES

Our official accreditations such as **CIR** allow clients to benefit from significant **R&D tax incentives**, streamlining their path to innovation.



RESPONSIBILITY

We uphold the highest standards of sustainability, with a strong commitment to Environmental, Social, and Governance (ESG) principles.



TRUSTED BY RESEARCH LEADERS

with an average satisfaction rate of 98,2% last year

Academic Institutions



Pharma / Biotech / CRO / CDMO



Cosmetics / Food





THE CARDIOVASCULAR DISEASES
EXPERTS



Preclinical CRO services for drugs targeting Cardiovascular diseases & cardiometabolic complications



Physio-pathological models
for *in vivo* studies



In vivo functional
exploration platform



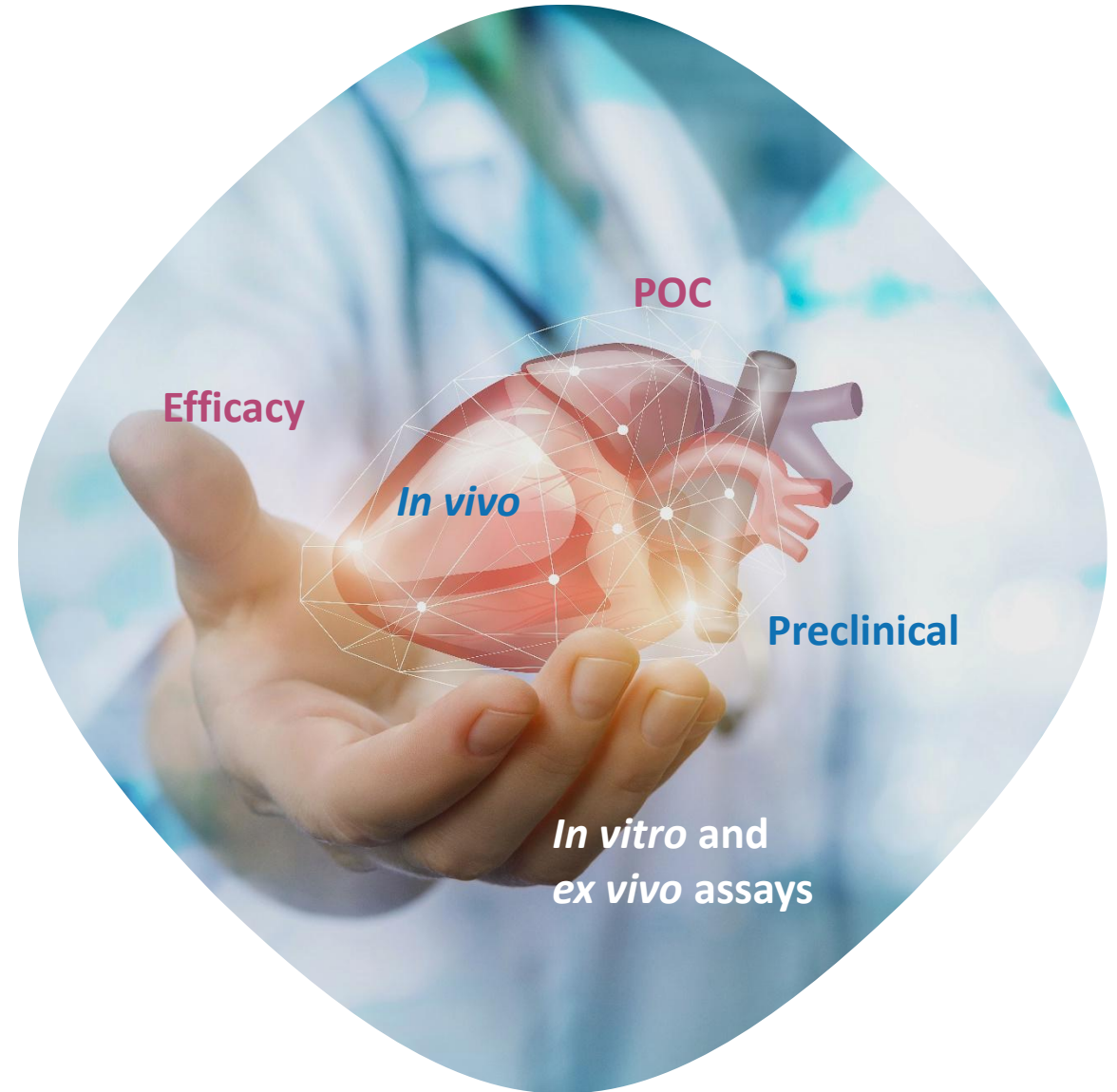
In vitro/Ex vivo
assays

We are

“

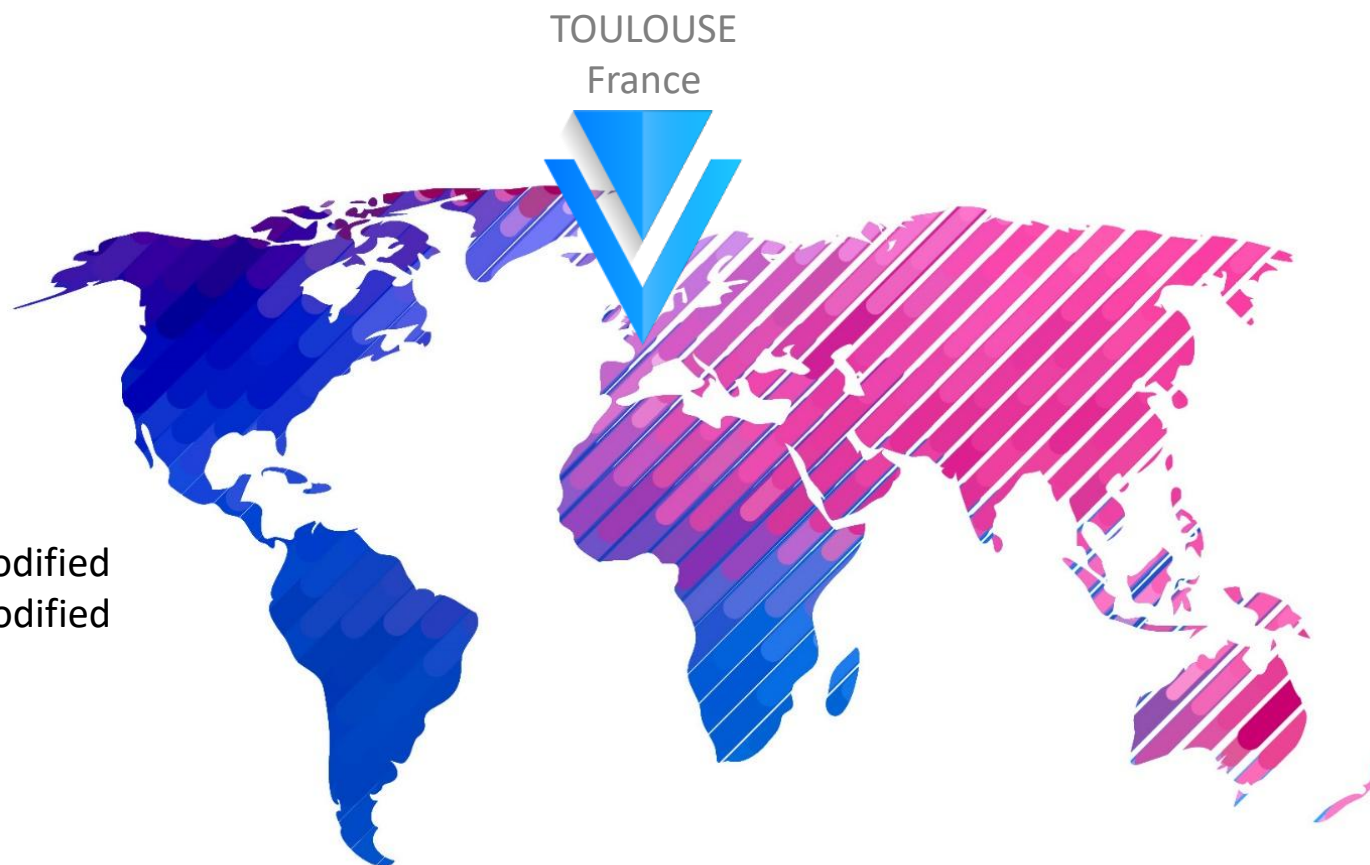
- A **CRO** specialized in **cardiovascular diseases** founded in 2011
- We provide **added-value expertise** to develop your **drug candidate** and deliver reliable results
- We offer a **wide variety of services** ranging from gold standard integrated patho-physiological models to isolated organs and cells

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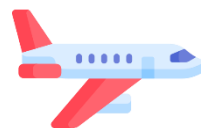


Our facilities

- Animal Housing area ISO-9001: **Rats, mice and hamsters**
 - SPF
 - SPOF
- Accredited by French/UE authorities to use genetically-modified organisms (adenovirus-associated vectors, genetically-modified animals, etc.)
- Research tax credit (CIR)



Direct access / easy connections



1h15 by plane from Paris
accessible by train from Paris



Cardiomedex with Janvier Labs

The perfect synergies for your drug development



Deliver early *in vivo* and *ex vivo* translational efficacy services to evaluate new innovative drugs for cardiovascular diseases:

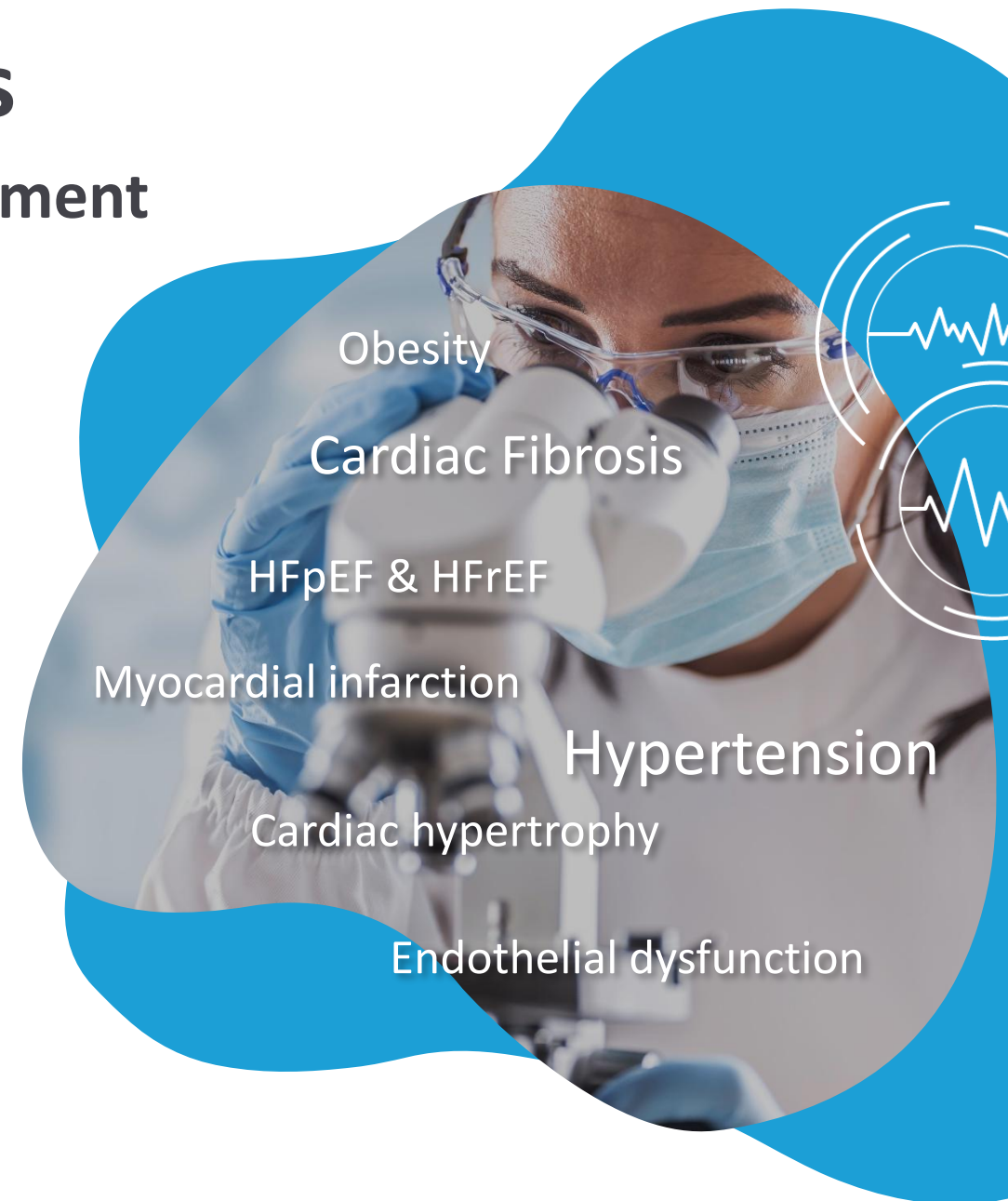
In vivo and *ex vivo* assays together with translational models with multiple common risk factors such as MASH, diabetic nephropathy, metabolic syndrome, hypertension and type 2 diabetes.



GOLD STANDARD PRECLINICAL MODELS

Create and breed translational disease rodent models to best evaluate drugs targeting metabolic disorders:

- Golden hamster
- B6 MASH
- OB/OB mouse
- DB/DB mouse
- Diet-induced B6 DIO



Cardiomedex and Physiogenex

Innovative twin sister-CRO companies
to evaluate your drugs on cardiometabolic disorders
And more recently...JC discovery



- Physio-pathological predictive models
- Customized preclinical pharmacology studies
- *In vitro, ex vivo, in vivo* exploration



Predictive models and in vivo exploration :
immuno-oncology, inflammation, auto-immune, and infectious diseases.



Benefits of our synergies

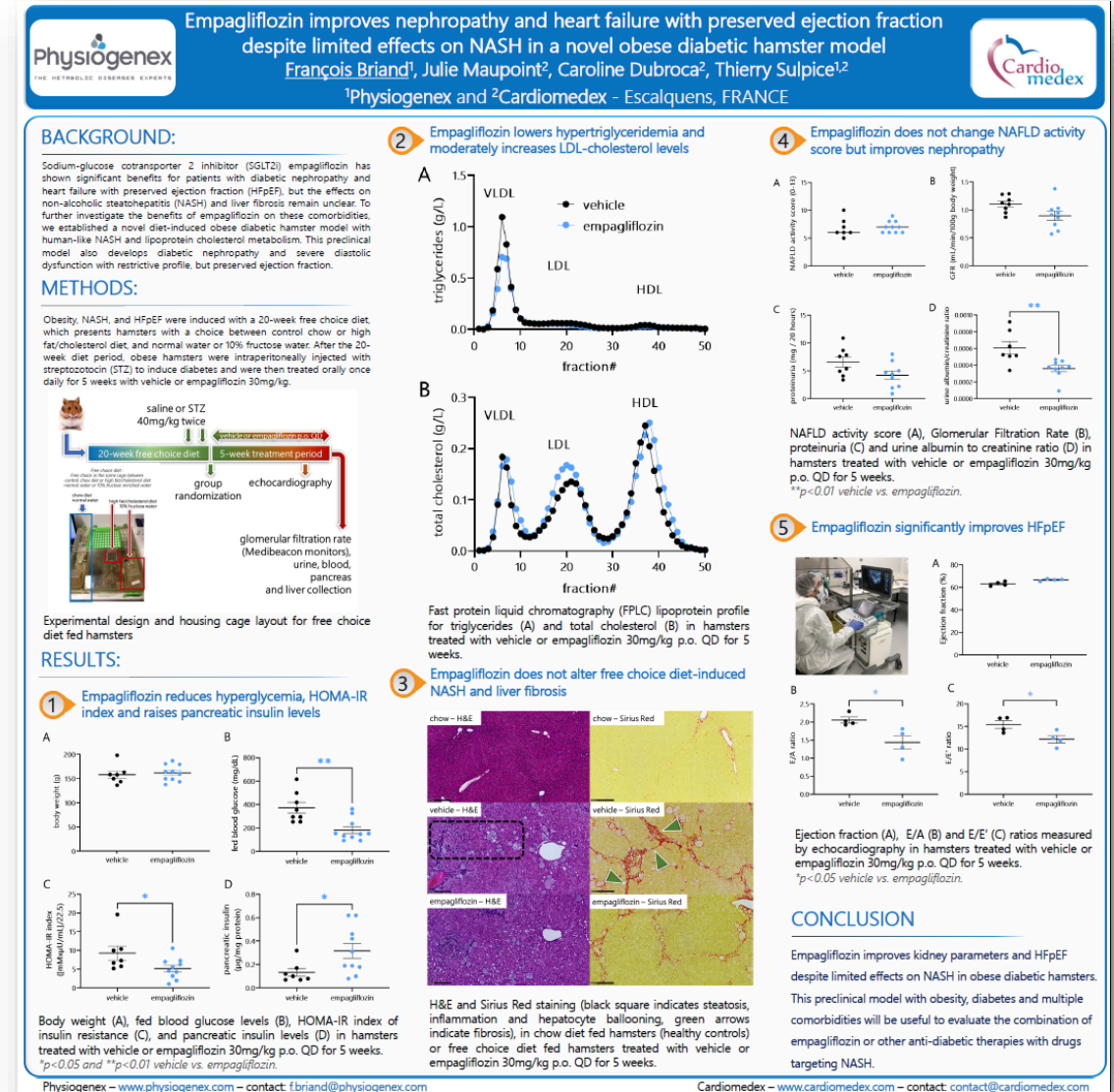
Example of unique synergy between **Cardiomedex**, **Physiogenex** and **Janvier Labs**

HIGH-VALUE RESULTS

Empagliflozin improves diastolic dysfunction in **Janvier Labs** **Golden Syrian hamster model of diabetes and diet induced NASH**.

This model shows severe heart failure with preserved ejection fraction (HFpEF) related to evident hepatocellular ballooning and portal/bridging (stage 2-3) fibrosis and develops alterations in kidney function as **characterized by our subsidiary company Physiogenex**.

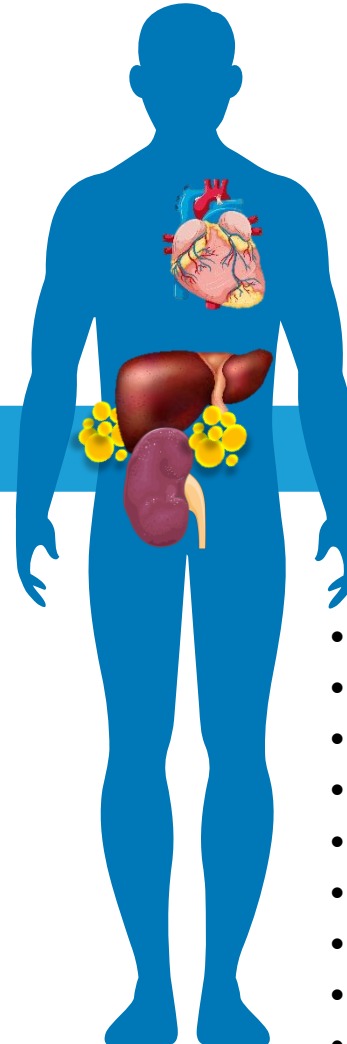
Empagliflozin became the first clinically proven therapy to improve outcomes for patients with HFpEF.



Derisk Translational data

Your drug development early and efficiently

- Diet-induced cardiometabolic diseases
- Genetic cardiovascular diseases
- Other cardiovascular associated diseases (aging, systemic inflammation, hypertension, obesity, diabetes, dyslipidemia, etc.)

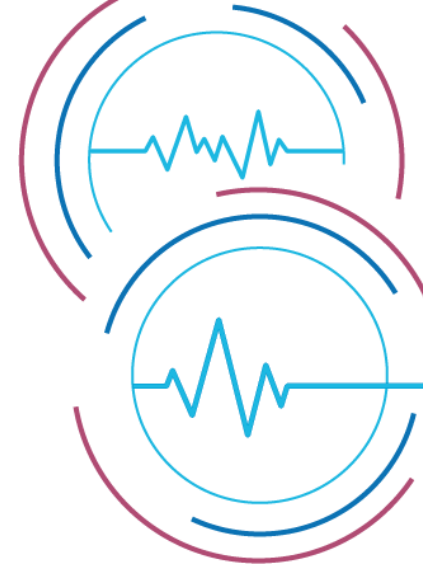


Marketed therapies

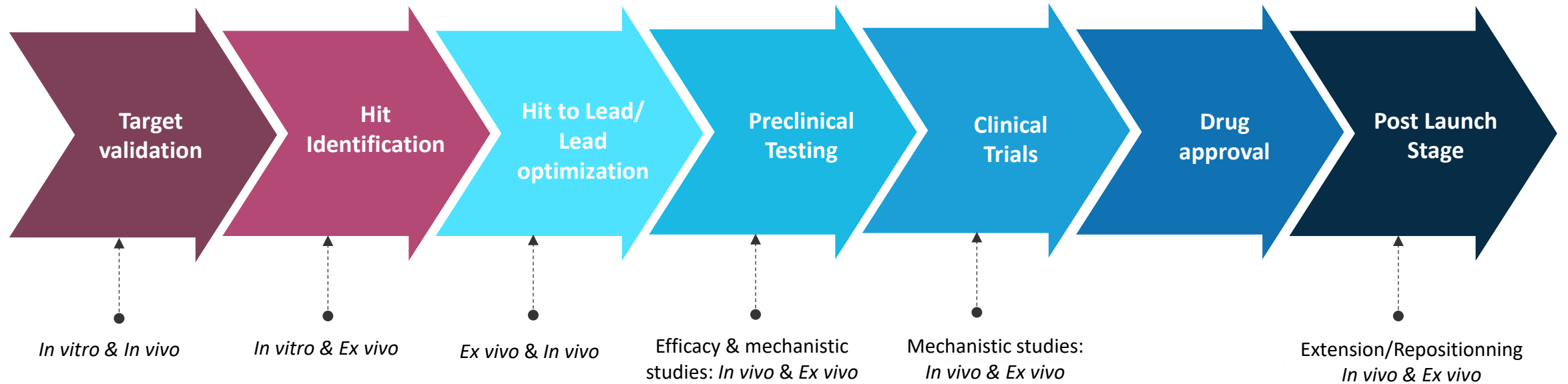
- Myocardial infarction and ischemia/reperfusion injury
- Heart failure with reduced ejection fraction (HFrEF)
- Heart failure with preserved ejection fraction (HFpEF)
- Cardiac hypertrophy
- Cardiac fibrosis
- Genetic (GMO models) and non genetic Cardiomyopathy
- Cardio-renal disease
- Aging
- Women's Health

Original & human-like animal models

Translatable efficacy parameters



Drug efficacy testing pipeline



THE BEST OPTIONS FOR YOUR LEAD COMPOUNDS

- Disease models development
- Comprehensive range of services

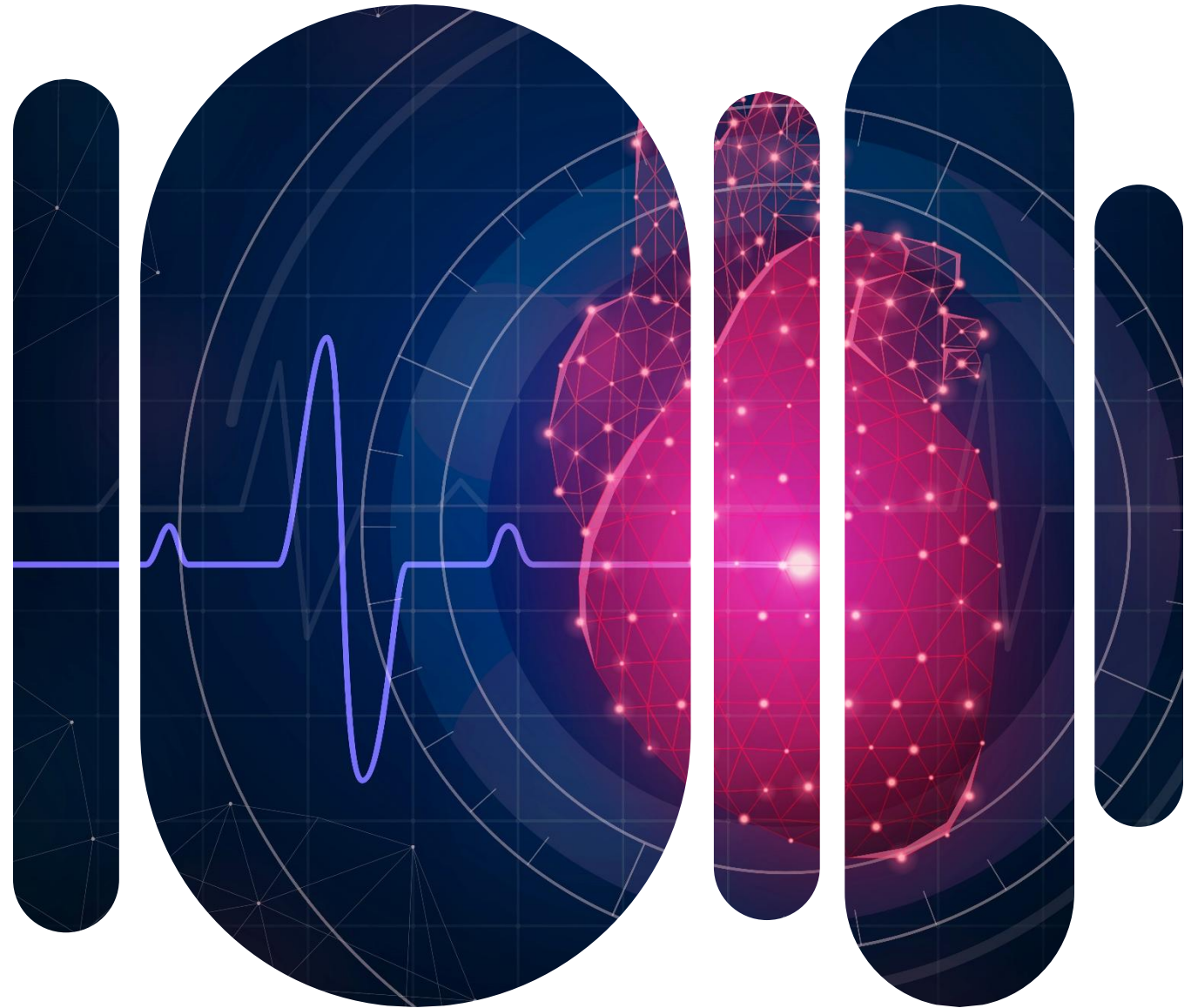


“

Our experts help you choose the best options

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DISEASE MODELS DEVELOPMENT



Therapeutic indications



Myocardial infarction induced heart failure with reduced ejection fraction (HFrEF)



Acute Myocardial Infarction



Heart failure with preserved ejection fraction (HFpEF)



Cardiac hypertrophy
Cardiac fibrosis



Genetic and non-genetic Cardiomyopathy



Takotsubo syndrome



Hypertension



Sepsis



Cardiometabolic and Cardio-renal



Aging



Women's Health

Innovative physio-pathological models

HFpEF

Hamster free-choice

Rat diet-induced obesity

Rat SDT fatty uninephrectomy

Mouse diet+L-NAME

Mouse diet-induced

Mouse Angiotensin-II $\pm$ HFD (young and old)

MASH mice

HFrEF

Rat/Mouse transaortic arterial constriction

Rat/Mouse permanent or transient artery ligation

Rat/Mouse transient artery ligation to test cardioprotective strategies

Cardiac hypertrophy/ Cardiac fibrosis

Rat/Mouse transaortic arterial constriction

Mouse Angiotensin-II $\pm$ HFD (young and old)

Cardiomyopathy

Mouse doxorubicin-induced toxicity

Genetic models

Mouse Takotsubo model

Hypertension

Spontaneously hypertensive rat

Rat Renal ligation

Sepsis

Lipopolysaccharide-induced models

Cecal ligation and puncture ligation

Takotsubo syndrome

Mouse Takotsubo model

Cardiometabolic/ Cardio-renal

Rat Diabetic Nephropathy

Mouse HFD+L-NAME

MASH mice

5/6 nephrectomized rat

Rat diet-induced obesity

Women's Health

HFD+AngII aged female

SDT female rat

PCOS models (under development)

Aging

Mice HFD + Ang II

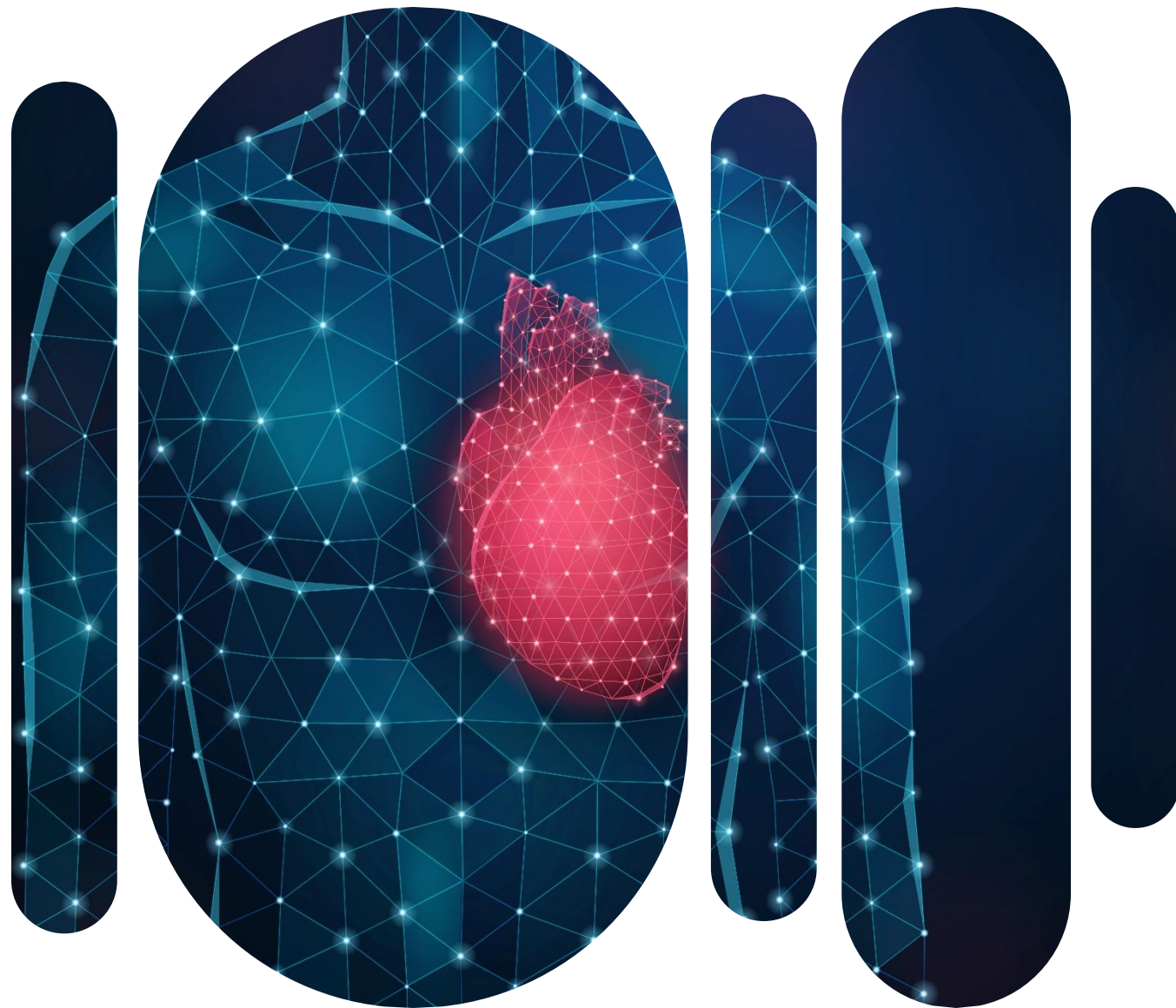


New model design

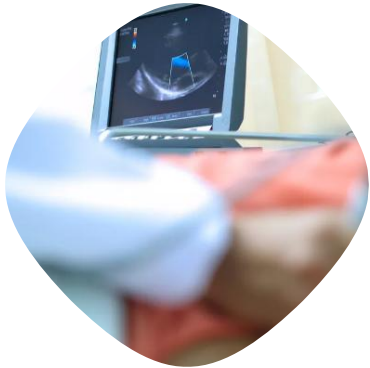
New preclinical models based on emerging areas to fulfil our partners' needs



COMPREHENSIVE RANGE OF SERVICES

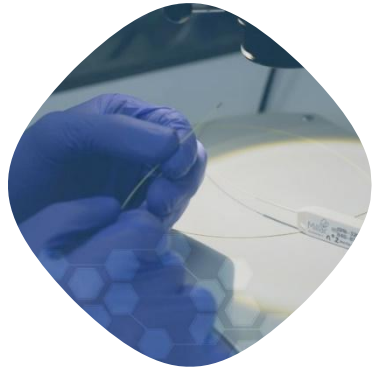


In vivo exploration of cardiovascular diseases



ECHOCARDIOGRAPHY

- **Gold standard** tool for comprehensive information about cardiac structure and function
- **Systolic and diastolic** function including M-mode, 2D, color, pulsed -wave Doppler, and tissue Doppler imaging.
- **Stress echocardiography**
- **Strain** analysis of left ventricle and/or left atrium
- **Left atrium** dimensions analysis
- **Pulmonary artery** flow analysis



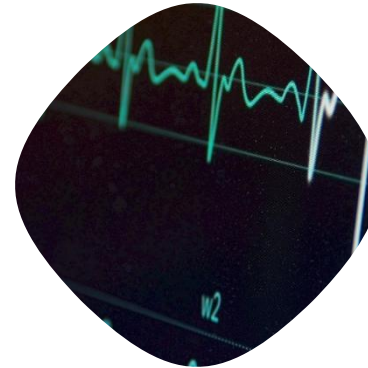
INVASIVE CARDIAC FUNCTION

- **Millar probes**
- Accurate **pressure measurements** within the left ventricle or real time left ventricular **pressure-volume loops**



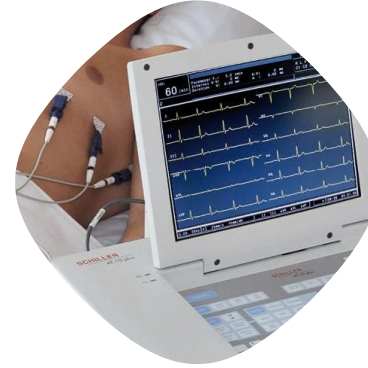
DOPPLER FLOW VELOCITY

- **Pulse Wave Velocity (PWV) measurements**
- Simultaneous Doppler velocity spectrogram acquisitions at two different locations
- Indicator for arterial stiffness



TELEMETRY MONITORING

- Conscious freely moving animals
- Measured parameters: blood pressure, heart rate, ECG, temperature, etc.



ELECTROCARDIOGRAM & HEART RATE VARIABILITY

- **Surface electrocardiogram** on anesthetized animals to measure the heart's electrical activity and highlight cardiac arrhythmias.
- **Heart rate variability**: quantitative markers of autonomic nervous system activity

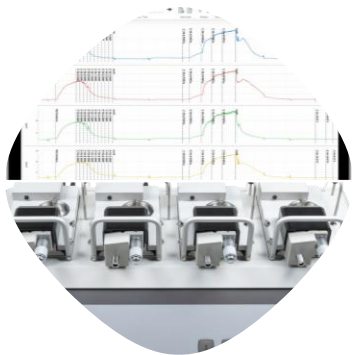


TREADMILL/CALO TREADMILL (In collaboration with Physiogenex)

- With an adjustable speed and slope, enable **forced exercise** training and accurate fatigue testing in rodents.
- Established for the **exhaustion test** on healthy mice, rats and hamsters as well as on our HFpEF models.
- Measurement of **indirect calorimetry parameters** (VO_2 , VCO_2 , RQ, and energy expenditure) during experimenter-defined activity profiles.

EX VIVO AND IN VITRO ASSAYS

FOR MYOCARDIAL CONTRACTILITY AND VASCULAR REACTIVITY EVALUATION



MYOGRAPH VASCULAR REACTIVITY, ENDOTHELIAL FUNCTION

- **Endothelial function** and **contractile properties** evaluation
- Isometric tension in **isolated arterial rings** from rodent measurement
- **Endothelium-dependent** or **-independent relaxation**



CELLULAR ASSAYS (under development)

- **Undifferentiated & differentiated cardiomyoblast**
- **iPSc cardiomyocytes**



LANGENDORFF PERFUSED ISOLATED HEART

- **Cardiovascular safety and efficacy** screening of new drug candidates
- **Cardio-protective effects** evaluation during ischemia-reperfusion



OROBOROS

- **Respiration measurement** at controlled oxygen levels
- **Redox biology** (NADH & CoQ)
- **ROS & ATP production, mt-Membrane potential** measurements

Complementary readouts

To fully characterize your drug candidates' mechanism of action and efficacy



Colorimetric assays

- Lactic acid – lactate dehydrogenase
- Creatine kinase
- Calcium
- Cholesterol, triglycerides, fatty acids
- ALT/AST
- Albumin
- Creatinine



ELISA and multiplex assays

- Hormones (pro-BNP, troponin I, insulin, etc.)
- Cytokines / chemokines panel (IL-1 β , IL-6, MCP-1, TNF α , IFN γ , MIP-1 α / β ; MIP-2, RANTES... etc.)



Western Blot analysis

- WES technology for any protein. on any sample/tissue.
- Protein (western blot) and Gene (qPCR) expression on any tissue:
 - Calcium signaling
 - Cardiac injury/overload
 - Cardiac hypertrophy
 - Glucose/fatty acid metabolism
 - ER and oxidative stress
 - Inflammation
 - Fibrosis



Histology analysis

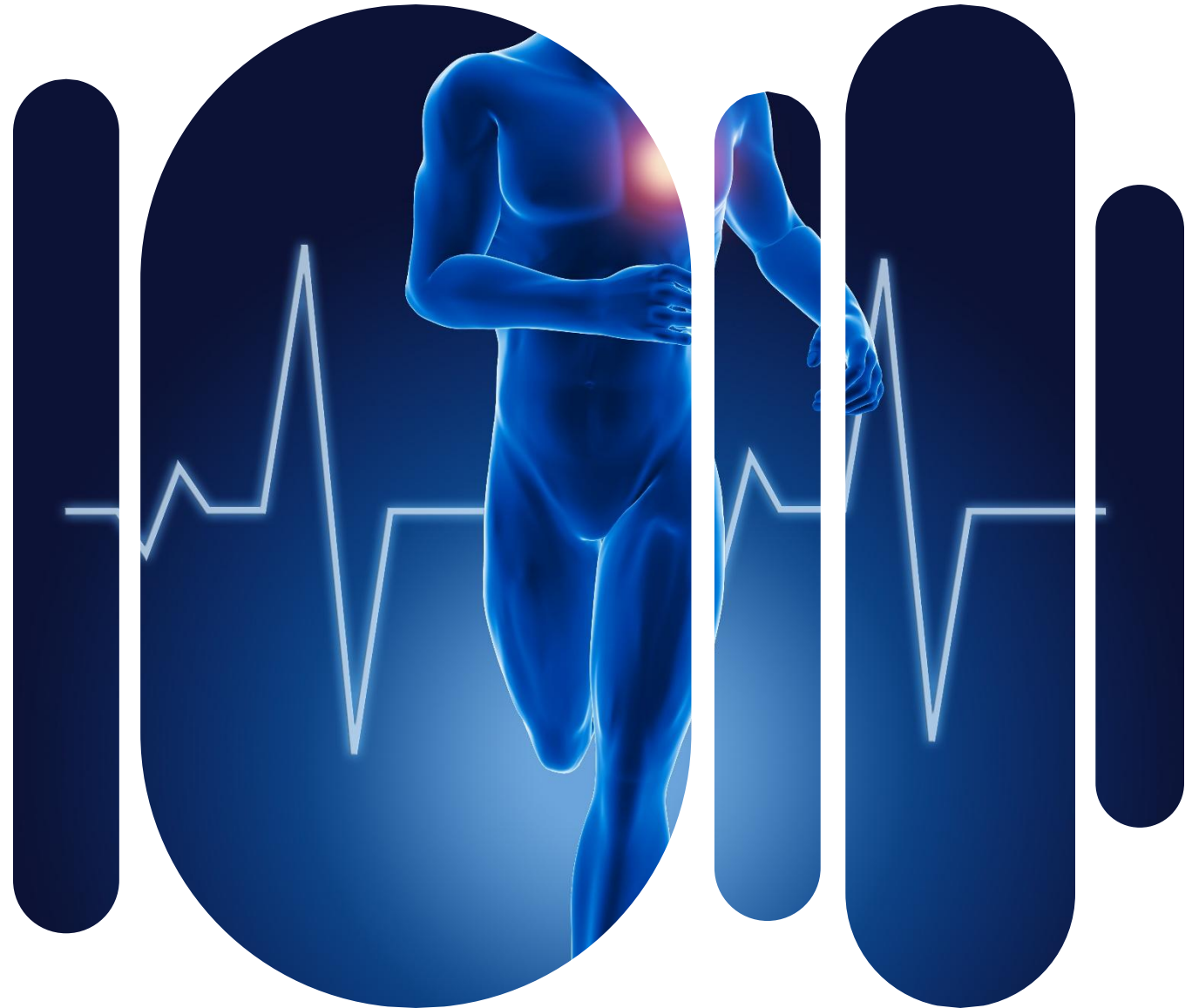
- H&E
- Sirius Red
- Masson Trichrome
- ORO
- PAS staining
- Immunohistochemistry (F4/80, CD68 ED1, collagen III alpha-SMA, etc.)
- NAS scoring (steatosis, inflammation, hepatocyte ballooning fibrosis)
- Nephropathy histopathology scoring (glomerulosclerosis interstitial fibrosis, etc.)



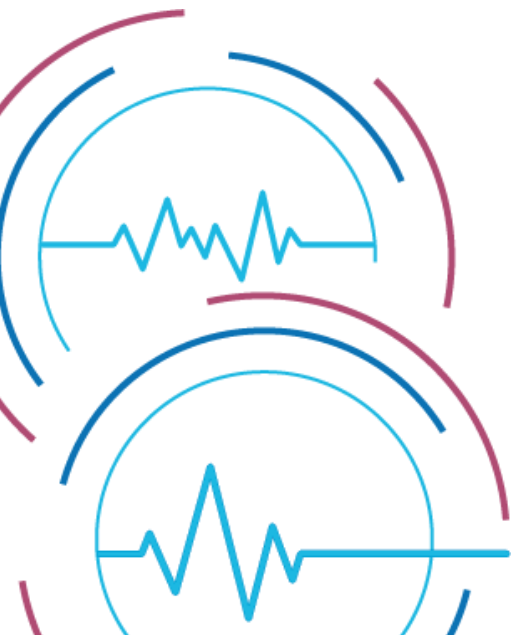
Pre-clinical pharmacology

- PK
- PD

PROVEN EXPERTISE



Publications showing Cardiomedex expertise in many scientific journals



> [Metabolism](#). 2021 Apr;117:154707. doi: 10.1016/j.metabol.2021.154707. Epub 2021 Jan 11.

Elafibranor improves diet-induced nonalcoholic steatohepatitis associated with heart failure with preserved ejection fraction in Golden Syrian hamsters

François Briand¹, Julie Maupoint², Emmanuel Brousseau³, Natalia Breyner³, Mélanie Bouchet³, Clément Costard², Thierry Leste-Lasserre⁴, Mathieu Petitjean⁵, Li Chen⁵, Audrey Chabrat⁶, Virgile Richard⁶, Rémy Burcelin⁷, Caroline Dubroca², Thierry Sulpice⁸

Affiliations + expand

PMID: 33444606 DOI: [10.1016/j.metabol.2021.154707](#)

> [Eur J Pharmacol](#). 2020 Sep 5;882:173316. doi: 10.1016/j.ejphar.2020.173316. Epub 2020 Jul 1.

Liraglutide shows superior cardiometabolic benefits than lorcaserin in a novel free choice diet-induced obese rat model

François Briand¹, Emmanuel Brousseau², Julie Maupoint³, Caroline Dubroca³, Clément Costard³, Natalia Breyner², Rémy Burcelin⁴, Thierry Sulpice⁵

Affiliations + expand

[.ejphar.2020.](#)

> [Dose Response](#). 2022 May 17;20(2):15593258221099281. doi: 10.1177/15593258221099281. eCollection 2022 Apr-Jun.

Highly Diluted Antibodies to eNOS Restore Endothelium Function in Aortic Rings From Hypertensive Rats

Nataliya V Petrova^{1 2}, Sergey A Tarasov^{1 2}, Oleg I Epstein^{1 2}, Caroline Dubroca³, Thierry Sulpice³

Affiliations + expand

PMID: 35602582 PMCID: [PMC9118459](#) DOI: [10.1177/15593258221099281](#)

> [Elife](#). 2023 Jan 17;12:e80904. doi: 10.7554/eLife.80904.

Ephrin-B1 regulates the adult diastolic function through a late postnatal maturation of cardiomyocyte surface crests

Clement Karsenty^{1 2}, Celine Guilbeau-Frugier^{1 3}, Gaël Genet⁴, Marie-Helene Seguelas¹, Philippe Alzieu⁵, Olivier Cazorla⁶, Alexandra Montagner¹, Yuna Blum⁷, Caroline Dubroca⁸, Julie Maupoint⁸, Blandine Tramunt^{1 9}, Marie Cauquil¹, Thierry Sulpice⁸, Sylvain Richard⁶, Silvia Arcucci¹, Remy Flores-Flores¹, Nicolas Pataluch¹, Romain Montoriot³, Pierre Sicard⁶, Antoine Deney¹, Thierry Couffinhal^{5 10}, Jean-Michel Senard^{1 11}, Celine Galés¹

Affiliations + expand

PMID: 36649053 PMCID: [PMC9844986](#) DOI: [10.7554/eLife.80904](#)

To make our **innovative new services and models** known for your drug evaluation success, early.

Enhancing NO pathway improves diastolic function in a hamster model of heart failure with preserved ejection fraction associated with nonalcoholic steatohepatitis

Caroline Dubroca¹, Julie Maupoint¹, Clément Costard¹, Emmanuel Brousseau¹, François Briand¹, Thierry Sulpire¹

¹Cardiomedex, Escalquens, FRANCE – contact@cardiomedex.com

BACKGROUND:

Heart failure with preserved ejection fraction (HFpEF) is a complex clinical phenotype frequently associated to the presence of multiple non-cardiac comorbidities including nonalcoholic steatohepatitis (NASH) commonly seen in metabolic syndrome and obesity. In this context, the enhanced production of ROS due to systemic inflammatory state participates to the myocardial structural and functional alterations by limiting nitric oxide bioavailability. We thus evaluated the effect of the phosphodiesterase type 5 (PDE5) inhibitor, vardenafil, on cardiac function and remodeling in a NASH hamster model.

METHODS

Male Golden Syrian hamsters were fed for 20 weeks with a free choice diet consisting in free access to control chow diet with normal drinking water or a high fat cholesterol diet with 10% fructose enriched drinking water. At 15 weeks hamsters were randomized on EIA ratio and ejection fraction to receive either vardenafil (10mg/kg/day orally for 5 weeks) or vehicle before cardiac and metabolic parameters evaluation.

RESULTS:

1 Vardenafil does not alter liver lipids and NASH in free choice fed hamsters

2 Vardenafil improves diastolic dysfunction in NASH hamsters

Representative H&E (A,B) and Sirius Red (C,D) pictures in lean and obese NASH hamsters after 20 weeks of diet. Dashed blue squares indicate microvascular structures, inflammation and hepatocyte ballooning. Green arrows indicate bridging fibrosis and collagen surrounding ballooned hepatocytes, which were clearly identified (dashed black squares) in obese NASH hamsters with CK-Mb immunohistochemistry (E-F). Liver lipids (G) and NAFLD activity score (H) in hamsters treated with vehicle or vardenafil.

CONCLUSION

The present data demonstrate that free choice fed hamster model of diastolic dysfunction characterized by relaxation impairments as well as higher filling pressure enhancing NO pathway with vardenafil treatment significantly improves diastolic dysfunction in NASH hamster model of HFpEF.



Cardio
medex
JANVIER GROUP



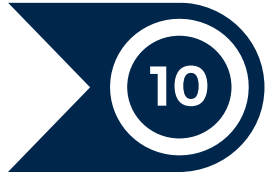
What if we work together?

Major steps ahead



- Interactive process
- Data secured and fully provided to customer
- Confidentiality/Intellectual property defined contractually

Partnering with us to launch your new therapies successfully



Over **10 years of experience/expertise** in drug development with major pharmas & biotechs.



Unique, **translational** preclinical models published in **major scientific journals**

Time and cost-effective preclinical studies to reach the clinical stage development

High added-value partnering with Physiogenex, Janvier Labs, JC Discovery and the other members within the Group to move your therapies successfully towards clinical stages.



As R&D studies providers, we propose and set-up **dedicated tools/animal models** to target your needs





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contact@cardiomedex.com



www.cardiomedex.com



Merci

