



Our expertise

Your success



Preclinical CRO

Efficacy

Discovery

Metabolic disorders

Innovative rodent models
and tailor-made
solutions

We are

An expert preclinical CRO delivering services for metabolic disorders and dedicated R&D studies to evaluate your drugs targeting, founded in 2003. We offer a wide range of tests to demonstrate the effectiveness of our clients' drug candidates.

ABOUT 20 YEARS OF EXPERTISE

specializing in **obesity, type 2 diabetes, MASH / MetALD, Fibrosis, diabetic nephropathy, neuropathy, metainflammation, dyslipidemia and cardiovascular diseases** for preclinical drug development, post launched studies and consulting.

We built our expertise over the years by developing innovative and predictive animal nutritional models to accelerate your drug discovery.



More than 10 of top 15 international biotech and pharma companies choose Physiogenex and gave the best chance of success to their lead compounds



Physiogenex and Cardiomedex

Innovative twin sister-CRO companies
to evaluate your drugs on
cardiometabolic disorders

Physiogenex

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

Cardio
medex

Diabetes

Cardio-renal
disorders

MASH
/ MetAID

Obesity

dyslipidemia /
atherosclerosis



Benefits of our synergies

INVENTIVA AND LANIFIBRANOR:
an example of unique synergy between
Physiogenex and Cardiomedex

HIGH-VALUE RESULTS

Lanifibranor improves NASH, fibrosis and diastolic dysfunction in a Golden Syrian hamster model of diet induced obesity and NASH.

This new study realized at Physiogenex generated data that further support the development of Lanifibranor as a treatment for patients with NASH who are at cardiometabolic risk.

This leading anti-NASH drug is now
evaluated in phase III (NATiv3).



Lanifibranor improves NASH, fibrosis and diastolic dysfunction in a hamster preclinical model of diet induced NASH



Wettstein G¹, Briand F², Sulpice T², Junien JL¹, Broqua P¹

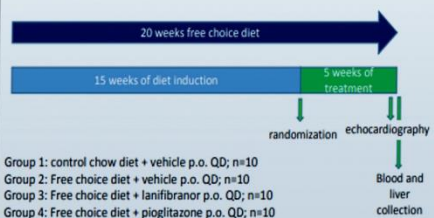
¹ INVENTIVA, Daix, France. ² Physiogenex, Escalquens, France

1-INTRODUCTION

Lanifibranor is a well-balanced agonist of the 3 PPAR isotypes with anti-inflammatory and anti-fibrotic effects in pre-clinical models of NASH. The NATIVE phase 2b trial (NCT03008070) in non-cirrhotic NASH patients demonstrated beneficial effects of lanifibranor treatment on several histological endpoints including NASH resolution and improvement of fibrosis. It has been reported in several studies that NASH increases the risk for cardiovascular diseases. Moreover, patients with NASH are at higher risk of developing diastolic dysfunction. We evaluated in this study the potential of lanifibranor in preventing metabolic changes and diastolic dysfunction in a preclinical model of NASH, in comparison with the PPAR γ agonist pioglitazone.

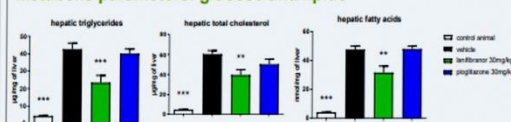
2-Material/Methods

Golden Syrian Hamsters under free choice diet (free choice between a chow diet with normal tap water or a high fat/cholesterol diet (Safe Diets) with 10% fructose enriched tap water) for a period of 15 weeks developed NASH, fibrosis and diastolic dysfunction compared to control hamster under chow diet. Hamsters were then treated for a period of 5 weeks with either vehicle, lanifibranor 30mg/kg or pioglitazone 30mg/kg. At the end of the treatment, liver histology, genes expressions and biochemical analysis were performed. Diastolic dysfunction was evaluated by echocardiography and defined as an absence of change in left ventricular ejection fraction, an increase in E/A and E/E' ratio and a decrease in E'/A' ratio as well as in isovolumic relaxation time (IVRT).

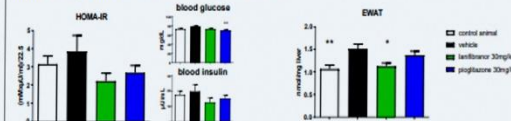


3-RESULTS

Metabolic parameters: glucose and lipids

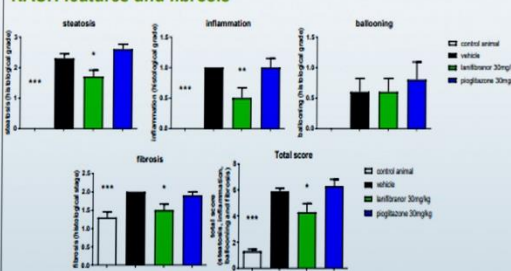


Lanifibranor, but not pioglitazone, significantly reduced epididymal white adipose tissue increase due to High Fat Diet.



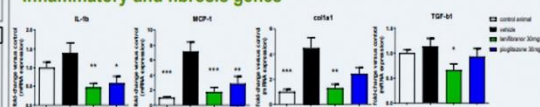
Lanifibranor, but not pioglitazone, significantly reduced epididymal white adipose tissue increase due to High Fat Diet.

NASH features and fibrosis

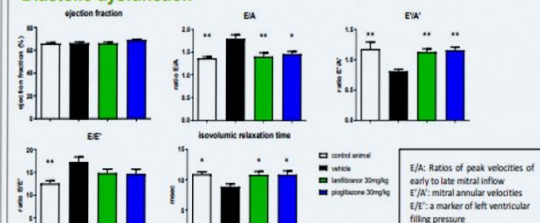


Lanifibranor, but not pioglitazone, significantly decreased steatosis, inflammation, fibrosis and consequently the total score taking into account the 3 NASH features and fibrosis.

Inflammatory and fibrosis genes



Diastolic dysfunction



4-CONCLUSION

Lanifibranor but not pioglitazone led to improvement in NASH and fibrosis suggesting that a panPPAR activation leads to a greater efficacy than a PPAR γ activation alone for the treatment of NASH-related liver features. Lanifibranor also markedly and significantly improved diastolic dysfunction similarly to pioglitazone. Activation of PPAR γ is therefore sufficient to correct the diastolic dysfunction in this model. However Lanifibranor as a pan-PPAR activator has the potential to limit the development of diastolic dysfunction via its beneficial effect on NASH but also by a direct effect on diastolic dysfunction through its PPAR γ component. This new data further support the development of lanifibranor as a treatment for patients with NASH who are at risk for cardiovascular diseases.

Contact information

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Guillaume.wettstein@inventivapharma.com

A management team of experience & expertise



Thierry Sulpice, Ph.D

CEO, CSO, Founder

- 9 years at Sanofi –Aventis
- In charge of drug discovery optimization and preclinical development for projects targeting the cardiometabolic syndrome.
- PhD in Physiology and Pharmacology – University of Grenoble, France.
- Founder and CEO/CSO of Cardiomedex



François Briand, Ph.D

**Director,
Research and Business Development**

- Expert in metabolic diseases since 2007.
- Worked with Novo Nordisk during his PhD in Nutrition and Metabolism, and with Glaxo Smith Kline and Merck as a postdoctoral fellow with Dr. Dan Rader at Upenn, Philadelphia.



Highly skilled metabolic disease experts working towards innovation, client satisfaction and quality compliance



Estelle Grasset, Ph.D – Project Manager



Natalia Breyner, Ph.D – Project Manager



Claire Bigot, Ph.D, Pharm.D – Project Manager, BD



Pr. Rémy Burcelin – Scientific expert consultant



Emmanuel Brousseau – Team manager



Marjolaine Quinsat – Animal welfare manager



Sura Setau – Quality department manager

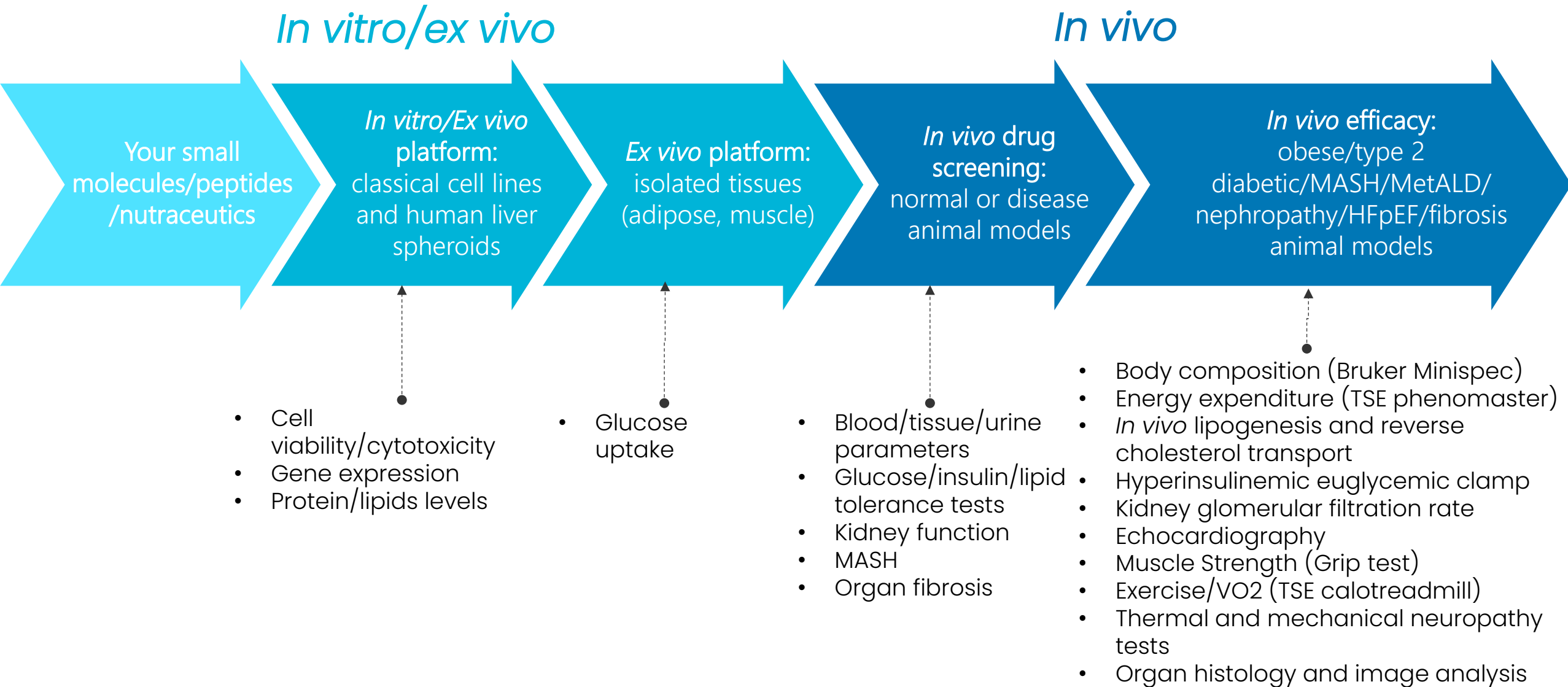


Julie Arasse – Administrative department manager

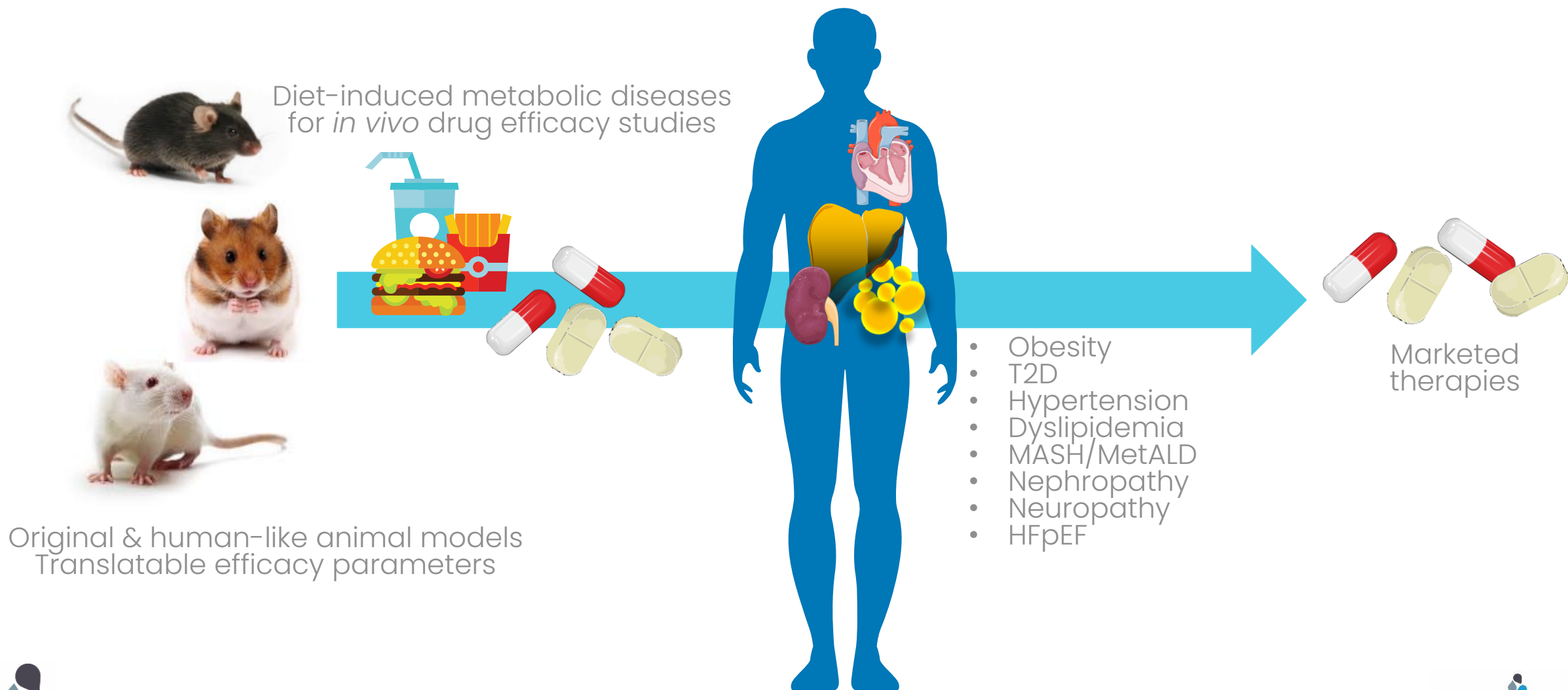
DRUG DISCOVERY | PRECLINICAL DEVELOPMENT



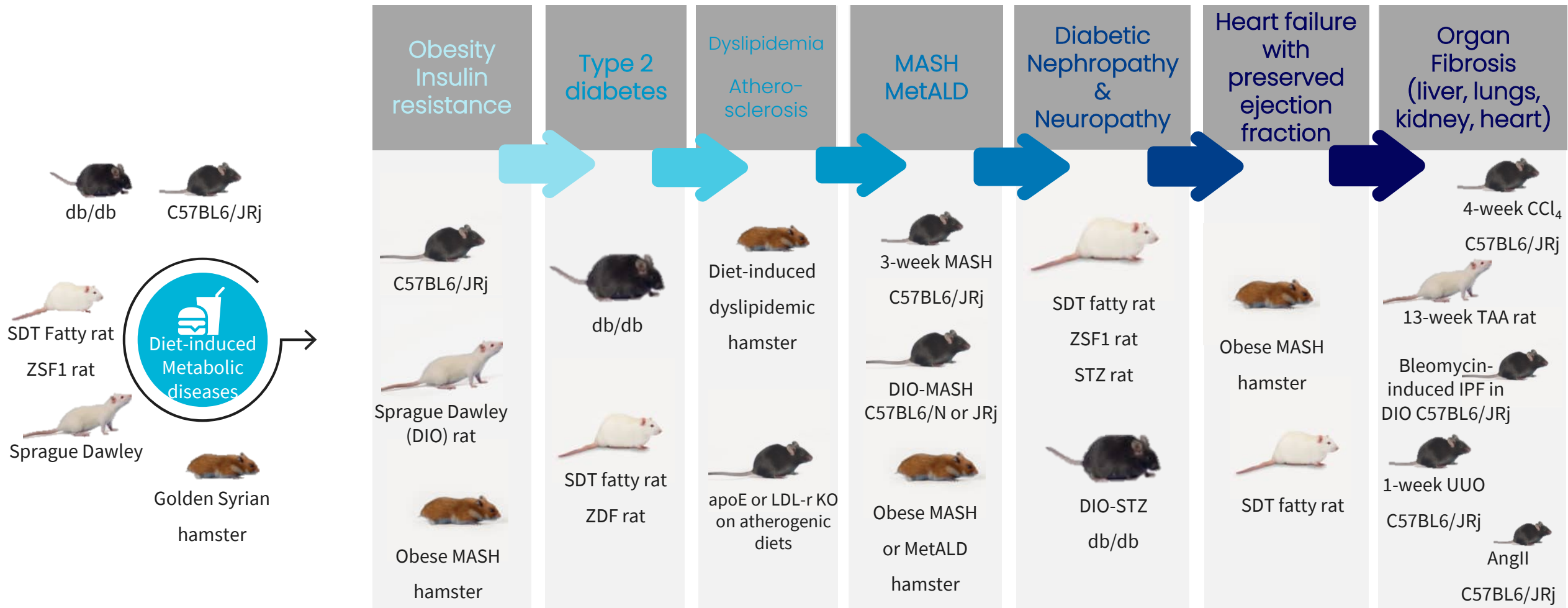
Drug efficacy testing pipeline



Translational data: Derisk your drug efficiently and early.



Innovative animal models developed to optimize and expedite your drug efficacy studies



Platform

To fully characterize your drug candidates mechanism of action and efficacy



Colorimetric assays

- Plasma and hepatic Lipids (cholesterol, triglycerides fatty acids)
- Lipoproteins (direct LDL-C and HDL-C assays, lipoprotein FPLC profile, apo A-1, apoB)
- Plasma ALT /AST
- Total ketone bodies
- Glycerol
- Phospholipids
- Albumin
- Creatinine
- Faecal total cholesterol and bile acids



ELISA and multiplex assays:

- Hormones (insulin, glucagon, adiponectin, Leptin, etc.)
- Cytokines panel (IL-1b, IL-6, MCP-1, TNF-alpha, etc.)



Western Blot analysis

(WES technology)
for any protein. on
any sample/tissue.



Microbiome, lipids, bile acids profiling RNAseq, RT-qPCR on any tissue:

- Lipogenesis
- Glucose 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.)

+ 50 publications demonstrating Physiogenex expertise in high impact scientific journals

Arteriosclerosis, Thrombosis, and Vascular Biology



JOURNAL OF THE AMERICAN HEART ASSOCIATION

Upregulating Reverse Cholesterol Transport With Cholesteryl Ester Inhibition Requires Combination With the LDL-Lowering Diet in Dyslipidemic Hamsters

François Briand, Quentin Thieblemont, Elodie Muzotte and T

Arterioscler Thromb Vasc Biol. 2013;33:13-23; originally published online doi: 10.1161/ATVBAHA.112.252932

Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 520 North Dearborn Street, Chicago, IL 60610-5901.

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European Journal of Pharmacology 860 (2019) 172537

Contents lists available at ScienceDirect

European Journal of Pharmacology

journal homepage: www.elsevier.com/locate/ejphar



Full length article

Nephropathy in diabetic db/db mice is accelerated by improved by the SGLT2 inhibitor dapagliflozin

Sisse Andersen Nørgaard^{a,c,1,*}, François Briand^{b,1}, Fredrik Wolfhagen Elisabeth Douglas Galsgaard^a, Henrik Søndergaard^a, Dorte Bratbo Sø

^a Pharmacology, Novo Nordisk A/S, Novo Nordisk Park, Måløv, Denmark

^b Physiogenex S.A.S, Prologue Biotech, 516 rue Pierre et Marie Curie, 31670, Labège, France

^c Department of Veterinary Disease Biology, University of Copenhagen, Grønnegårdsvej 15, 1870, Frederiksberg C, Denmark

2032

François Briand,¹ Eric Mayoux,² Emmanuel Brousseau,¹ Noémie Burr,¹ Isabelle Urbain,¹ Clément Costard,¹ Michael Mark,² and Thierry Sulpire¹

Empagliflozin, via Switching Metabolism Toward Lipid Utilization, Moderately Increases LDL Cholesterol Levels Through Reduced LDL Catabolism

Diabetes 2016;65:2032–2038 | DOI: 10.2337/db16-0049

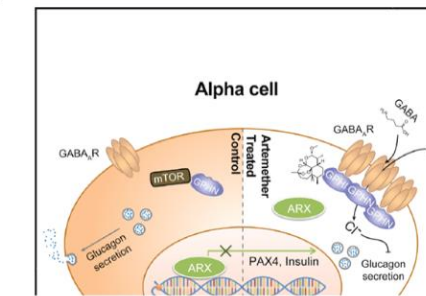
Diabetes Volume 65, July 2016



Cell

Artemisinins Target GABA_A Receptor Signaling and Impair α Cell Identity

Graphical Abstract



Authors

Jin Li, Tamara Casteels, Thomas Frogne, ..., Patrick Collombat, Jacob Hecksher-Sørensen, Stefan Kubicek

Correspondence

skubicek@cemm.oew.ac.at

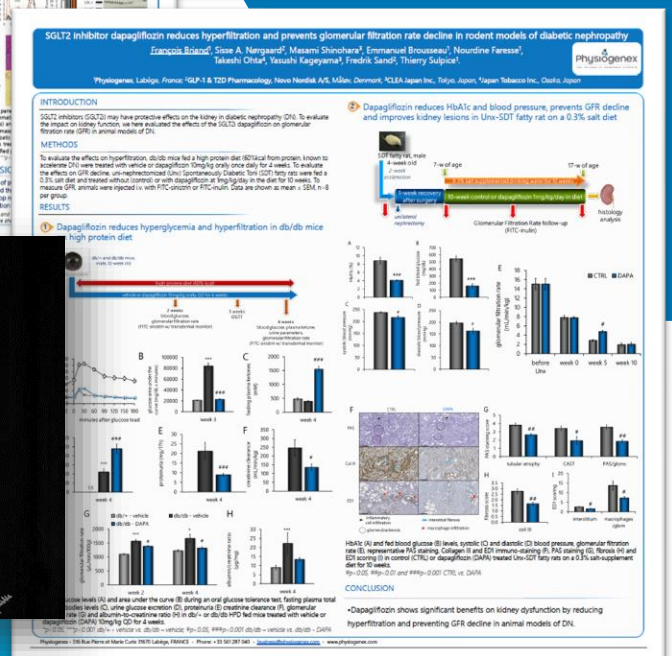
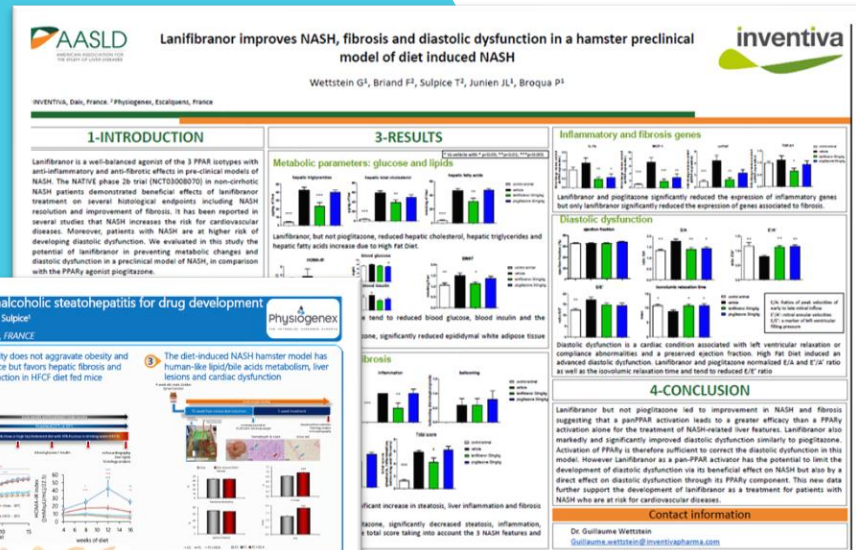
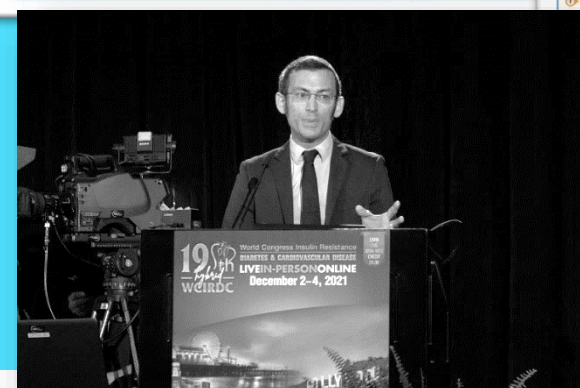
In Brief

The anti-malarial drug Artemisinin can drive the in vivo conversion of pancreatic α cells into functional β -like cells through enhanced GABA signaling and may have potential as a therapeutic for diabetes.

+150 POSTERS and TALKS

in international conferences

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



They trust us

ILDONG 일동제약

 altimmune



GlaxoSmithKline



Boehringer
Ingelheim



teva

achē



BIOCODEX
healthcare with passion and conviction



Genentech
A Member of the Roche Group



ENANTA
Pharmaceuticals



AMGEN



High success rate customer satisfaction over the last 4 years: 97.5%

« I can't thank you enough for all your great work and support! It was really nice collaborating with you all and I am very much looking forward to the next collaboration with you! »

– US Pharma customer

« Great working with Physiogenex: great competence in the area, straight answer and very good team available to support all our needs »

– European biotech customer

“Once again, I would like to appreciate for all your assistance during the study execution and all technical issues that Physiogenex experts helped us to understand. Physiogenex is a very strategic partner and in the future, we certainly will consider you to perform our preclinical studies.” – South American Pharma customer



When is your turn?

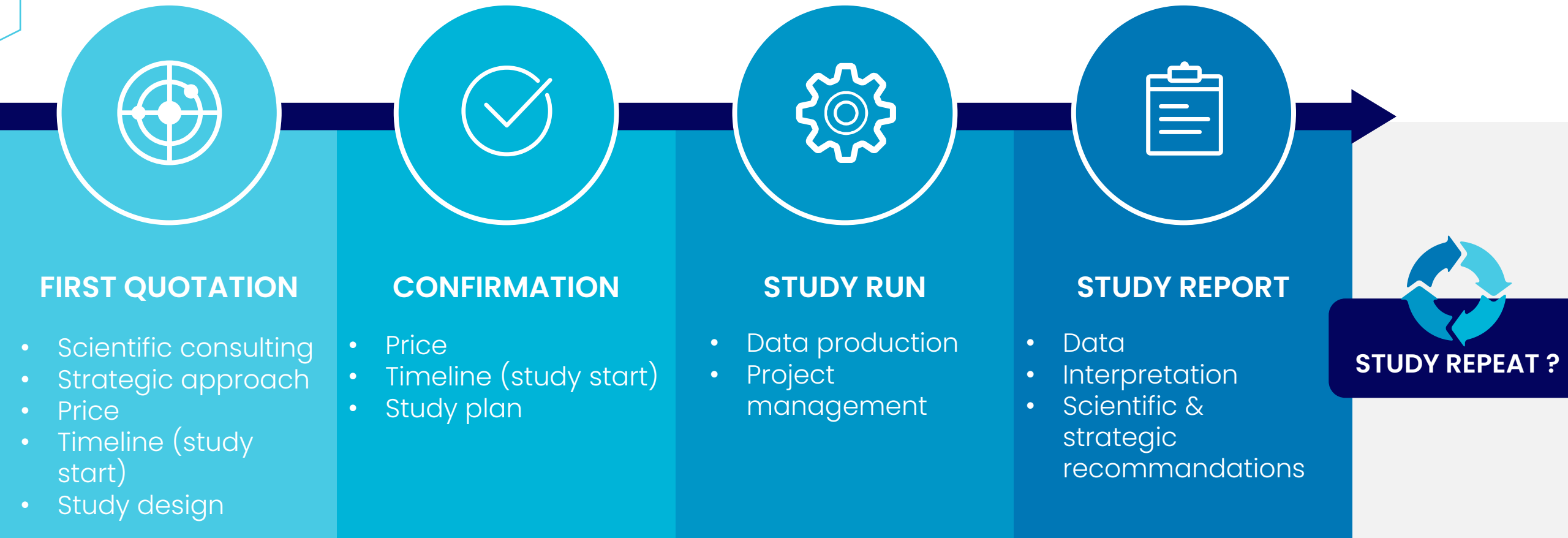
“Excellent scientific advice provided for the study design. Studies tailored for small biotechs with limited budget. Timelines met, rigor in execution. Indeed a great partner for drug development in the metabolic disease area.” – US biotech customer

*“High level of expertise and timely discussions during the study plan and execution
Very co-operative” – India Pharma customer*

“We really appreciate what you did for our study. A new assay development was successful. The study report was well-documented.” – Korean Pharma customer

What if we work together?

Major steps ahead



Quotation and study confirmation

1. Discussion with our experts to setup the best cost-effective study design for your drug efficacy project
2. An experimental design and quotation are then proposed with study timelines
3. Upon you agreement, a study plan is issued and once signed your study starts (2-3 weeks average)



Code of study: xxx004
Version: final

Physiogenex
THE METABOLIC DISORDERS EXPERTS

The financial quote is based on information provided in the study plan.
All our prices include the study/project management, exploitation and interpretation of raw data as well as finalization of a final report with scientific recommendations and conclusions.
Note: after study start, any additional request that are not specified in the study plan will be subject to additional charges.

Date of issue: February the 16th, 2021

Description	Quantity	Total
Golden Syrian Hamsters, male, 4-week old (n=47), shipment, identification, housing (acclimation and 15-week free-choice diet induction periods), specific diet and weekly body weight, blood collection, screening procedure (TC, ALT, AST, HOMA-IR and body weight), histology analysis (H&E, Sinus red, % Sinus Red labelling and NAS) at baseline (n=5 hamsters)	47	
Housing (5-week treatment period), specific diet and weekly body weight/food and water intake, semaglutide, formulation preparation, subcutaneous Q3D dosing for 5 weeks, echocardiography for left ventricular function and dimensions, blood collection, heart, lungs and tibia collection, weight and fixation	42	
HOMA-IR, plasma TC, TG, ALT, AST and IL-6, hepatic total cholesterol, triglycerides and fatty acids, hepatic gene expression (IL-1b, MCP-1, TGF- β , coll1a1, TIMP1, SREBP-1c, SCD1, FASN, ghREBP, FGF21), histology analysis (H&E and Sinus Red), % Sinus Red and NAFLD activity score	42	

TOTAL (taxes non included)

Payment process: 50% when signed: _____
50% when delivered: _____

optional items	Quantity	Total
UCP1 gene expression in brown adipose tissue and inguinal adipose tissue	42	

Validity : 3 months

Sponsor Representative	Date	Signature

Version : 8

DOCUMENT STRICTLY CONFIDENTIAL
Physiogenex SAS
Phone : 33 5 32 09 79 80 - contact@physiogenex.com
S.A.S. au capital de 39110 € - APE 7211Z

Ref. Doc : EDOC002-4





Study run

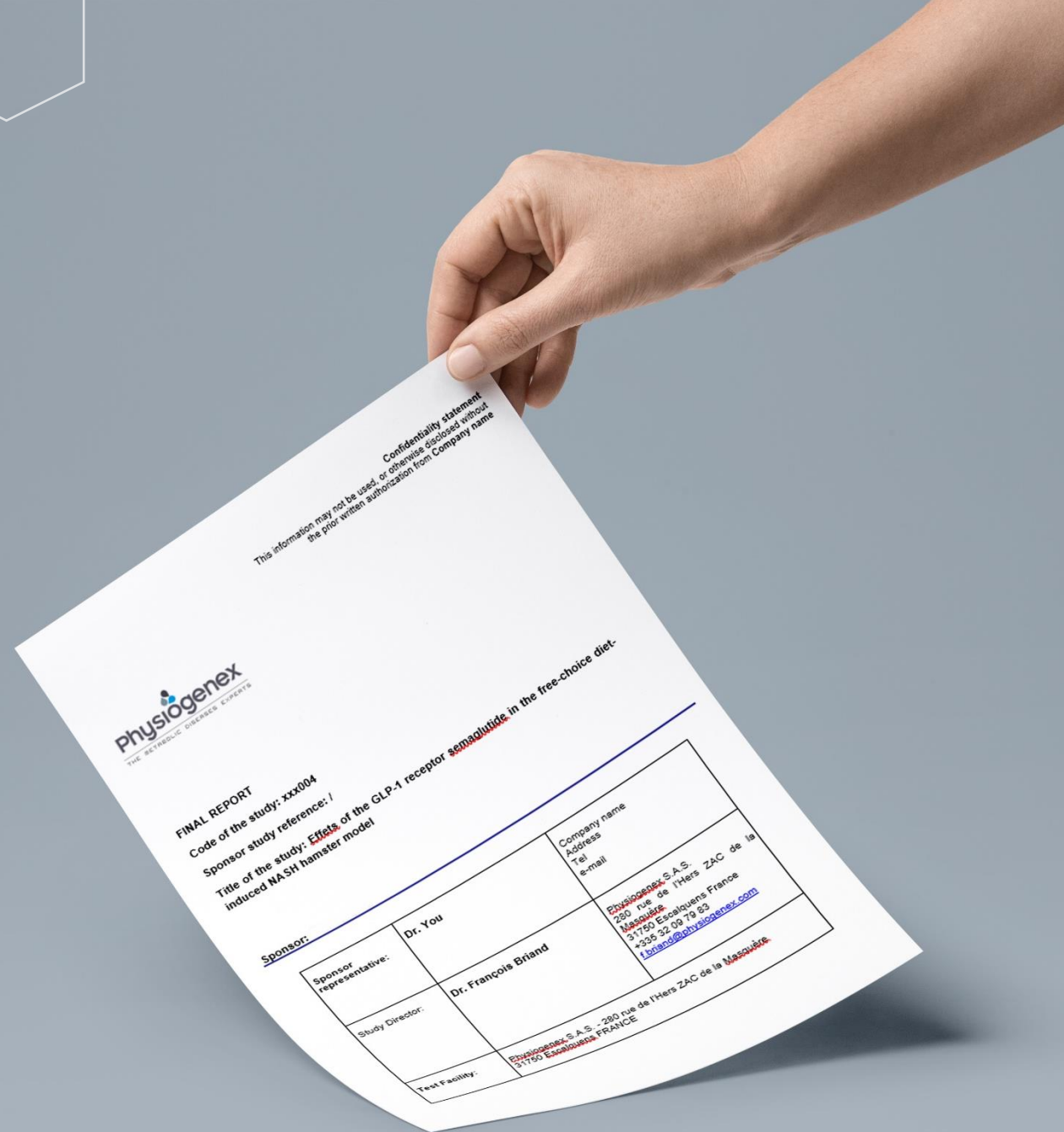
- ✓ Studies led by a dedicated project manager
- ✓ Fast and efficient communication: Weekly follow-up
- ✓ Raw data delivered as soon as available





Study report

- ✓ A clear description of your study results provided on Word format for your review
- ✓ Includes statistical analysis, data expertise and recommendations to go further with your drug development
- ✓ Reporting includes quality-controlled data on Excel format, statistics (GraphPad)



Partnering with us to launch Your new therapies successfully

Obesity – Type 2 diabetes – Dyslipidemia
MASH/MetALD – Diabetic nephropathy & neuropathy,
dyslipidemia, atherosclerosis and HFpEF

- Over 20 years of experience/expertise in drug development with major pharmas & biotechs
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- 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 Cardiomedex
- As R&D studies providers we propose and set-up dedicated tolls/animal models to target your needs



Physiogenex and you



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