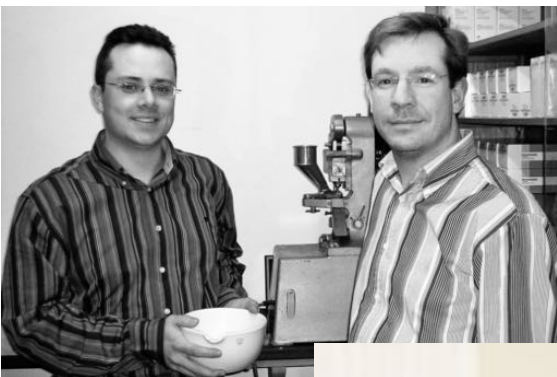




BioNotus Company Presentation June 2023



**AFTER  
DECADES OF  
EXPERIENCE**















*anno 2005*

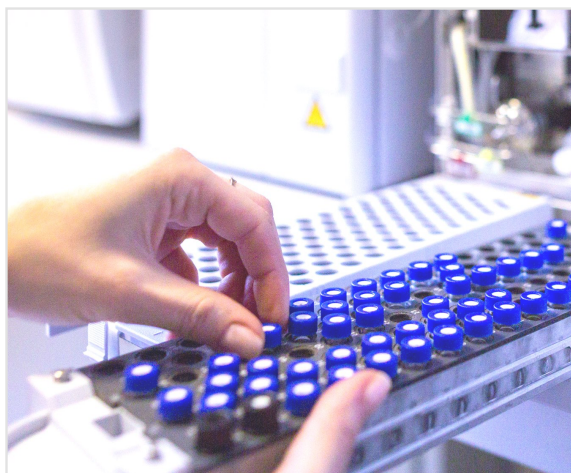


Prof. Pieter Annaert

Pharm. Johan Van Daele

- May 2017**  **Establish Company**  
Founded by Pieter Annaert & Johan Van Daele
- Oct 2017**  **First bioanalysis method validated**  
Sildenafil
- Aug 2018**  **Waste water project tackled in 3 weeks**  
while established labs were trying 3 years
- Apr 2019**  **Launch of IMI project ConcePTION**  
Participating in bioanalysis and M&S
- Nov 2019**  **Bile acids multiplex method validated**  
**Launch cancer vaccine project**
- Dec 2019**  **Co-design of study and bioanalysis**
- Feb 2020**  **VLAIO grant supports BioNotus' Pharmacometrics strategy**
- Apr 2020**  **IntiQuan Alliance & Thomas Bouillon joining**
- Dec 2020**  **Best-in-class Meropenem method**  
**Paracetamol-Morphine 9-plex method**
- Feb 2021**  **Discovery ADMET operational**
- Jul 2021**  **Design for clinical study (inhalation)**
- Mar 2022**  **Neurotransmitters in zebrafish, Lipid nanoparticles characterisation,...**

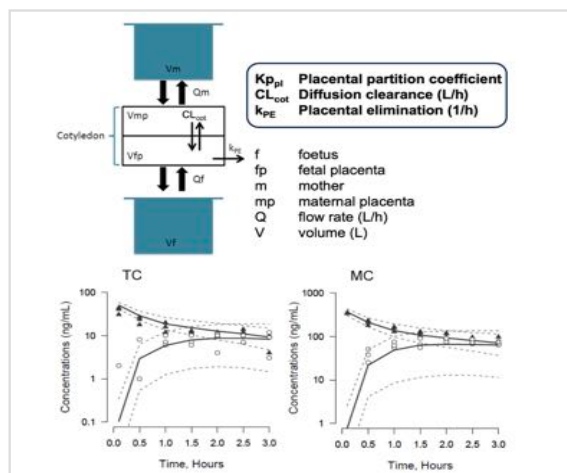
# BioNotus Capabilities



## BIOANALYSIS

### DRUGS AND BIOMARKERS

Bioanalysis encompasses the absolute and reproducible quantification of drugs, their metabolites and biomarkers in a range of biological matrices (blood, plasma, saliva, urine, CSF,...)



## PHARMACOMETRICS

### MODELLING & SIMULATION (M&S)

Both top-down and bottom-up computational approaches enable prediction of individualised dosing and elucidation of underlying mechanisms relating to pharmacokinetics, efficacy and toxicity



## DISCOVERY ADMET

### EARLY PK PREDICTIONS

*In vitro* models of liver, lung, kidney, intestine, breast and brain support determination of drug-specific PK parameters from the drug discovery stage onwards.

# *Fit for Purpose* is our DNA

---



## **RESEARCH QUESTION**



... identifies the specific objectives and drives the project flow

## **CONTEXT-OF-USE VALIDATION**



... for cost-efficient and sustainable quality management

## **SMALL TO LARGE SAMPLE SETS**



... to draw the best possible conclusions

## **EMA, ICH and FDA GUIDELINES**



... to meet regulatory requirements

## **ITERATIVE INTEGRATION**



... of Bioanalysis and PMX to turn data into actionable insights

## **DIVERSE PARTNER NETWORK**



... to always select the best possible team and solution





Typical research questions (clinical / non-clinical)

# Bioanalysis: **purpose**

- Quantitative determination of plasma concentrations of **small molecules and their metabolites, large molecules and biomarkers**, in all phases of your drug development.
- Preclinical toxicity studies from 2023 Q4 (**GLP** certification)
- Pharmaceutical analysis: examples:
  - **RNA vaccines**: LNP-Drug product characterisation: content, impurities, forced degradation studies.
  - Mapping of **glycosylation of drug product** with HRMS
  - Quantification of **nitrosamines** in drug product and its mutagenic metabolites (drug dosage approval)
- Quantitative determination of 4 $\beta$ -hydroxy-cholesterol/cholesterol ratios in plasma as *in vivo* **biomarker** for hepatic CYP3A activity

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BIOANALYSIS



PHARMACOMETRICS

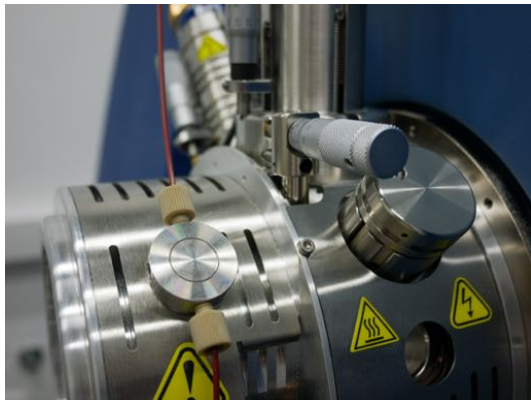


DISCOVERY ADMET



Typical research questions (clinical / non-clinical)

# Bioanalysis: means



BIOANALYSIS ★ PHARMACOMETRICS ★ DISCOVERY ADMET ★



Typical research questions (clinical / non-clinical)

# Pharmacometrics: **purpose**

- **Dose-Exposure-Response** relation of your drug?
- **Right dose** for the **next clinical phase** of your drug candidate?
- **Mechanisms** of Absorption, Distribution, Metabolism and Excretion (**ADME**)?
- Gaining insight into **(patho)physiological** mechanisms
- Predicting **drug-drug interactions** (DDI)
- Predicting PKPD in **special populations**
- **Communicating** M&S added value and results to domain experts

BIOANALYSIS



PHARMACOMETRICS



DISCOVERY ADMET



Typical research questions (clinical / non-clinical)

# Pharmacometrics: means

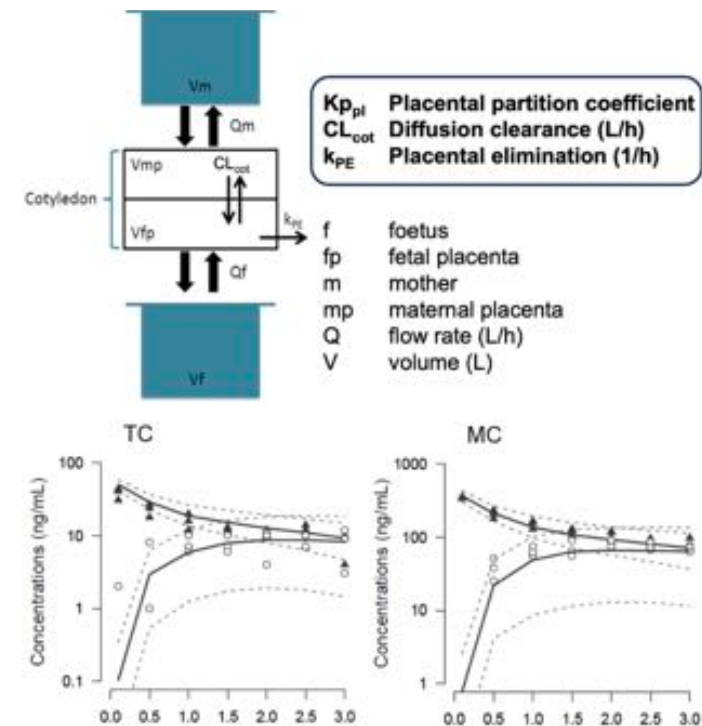
- Top down PKPD modelling of clinical data and animal data
  - population approach support sparse data analysis
- Bottom up PBPK(PD) modelling for drug candidates
  - Physiology based pharmacokinetic modelling relies on *in vitro* to *in vivo* extrapolation (IVIVE)
- Physiology-based Biopharmaceutics Modelling (PBBM)
- Semi-Mechanistic modelling, middle-out approach
- Using industry standard software platforms for M&S
- Strategic collaboration with Intiquan (Basel, CH)

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BIOANALYSIS

★ PHARMACOMETRICS

★ DISCOVERY ADMET





Typical research questions (clinical / non-clinical)

# Discovery ADMET: **purpose**

- Predicting the **hepatic clearance** (e.g. by metabolism) of your drug candidate
- Identifying the roles of **metabolising enzymes** and **transport proteins**
- **Metabolite profiling**: generate and identify drug metabolites
- Determine the **plasma protein binding** of your drug
- Determine the impact of your drug on **hepatic bile acid processing**
- Reveal and predict drug-drug interaction (DDI) potential
- Transport across the blood/milk barrier & the placenta

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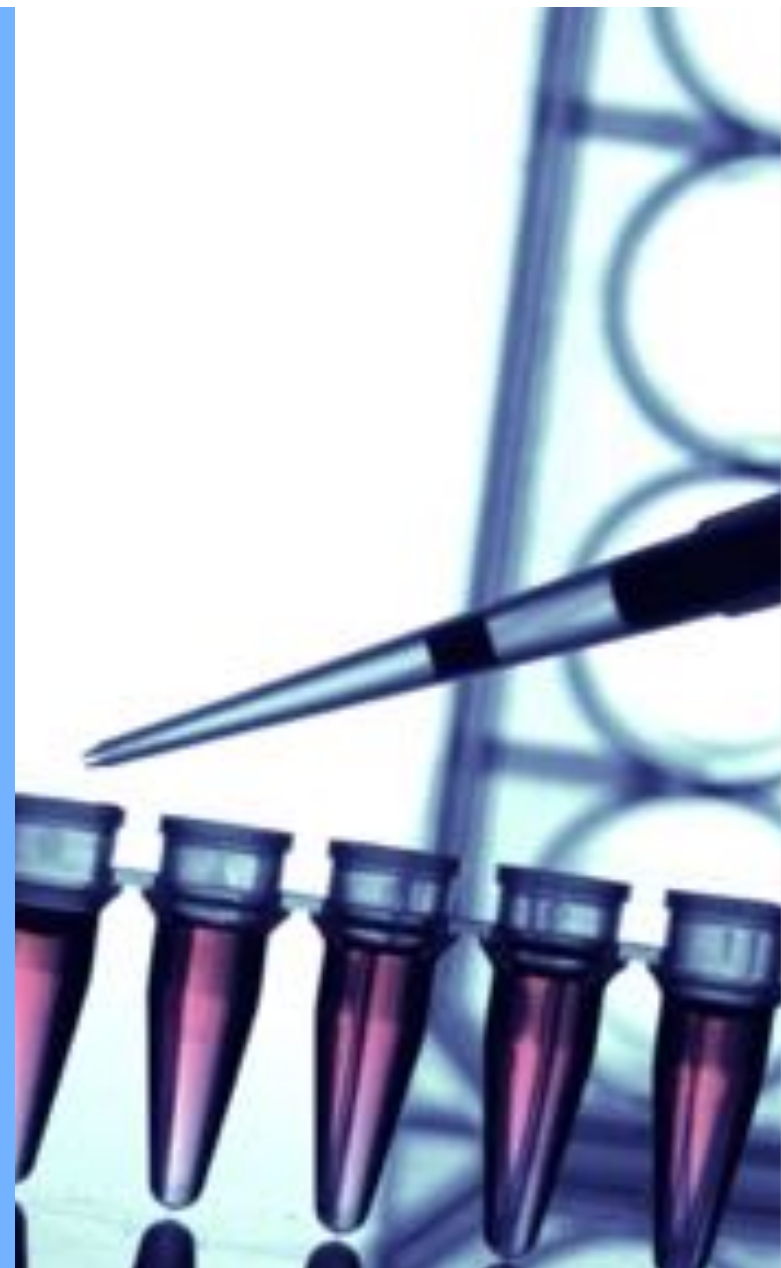
BIOANALYSIS



PHARMACOMETRICS



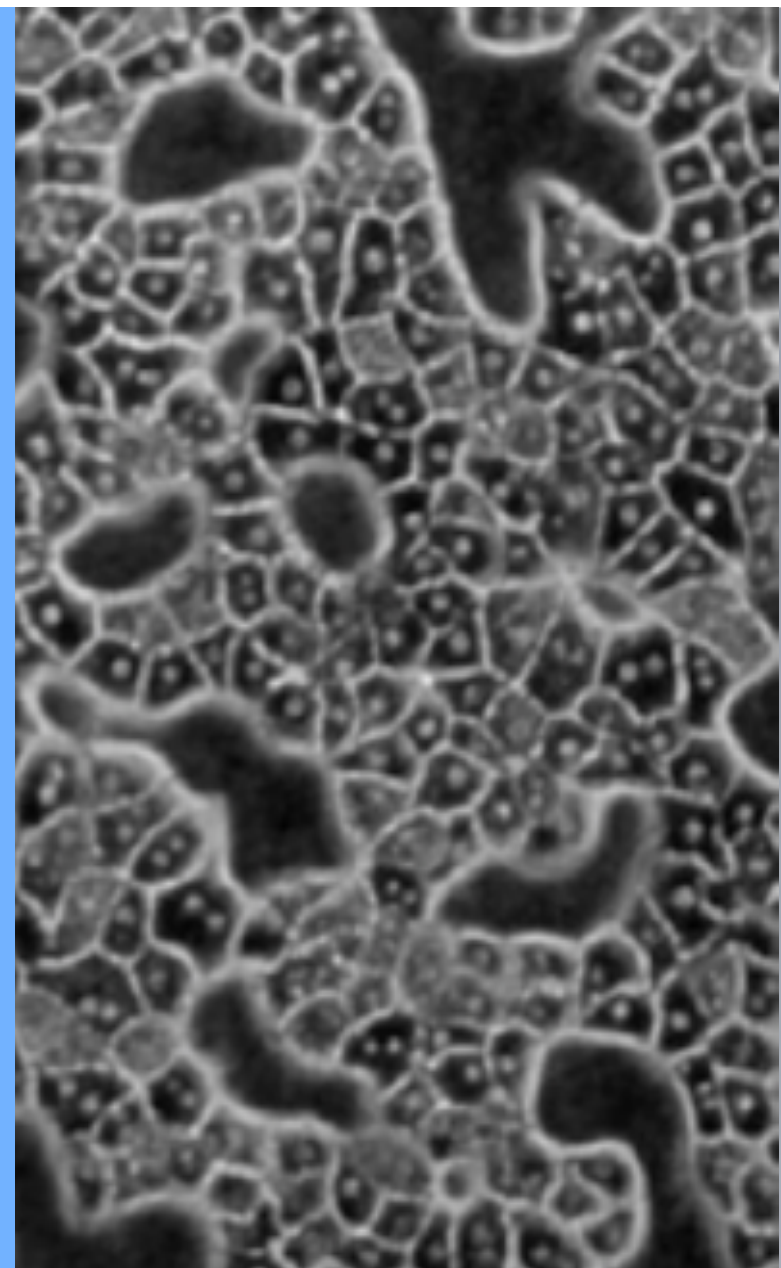
DISCOVERY ADMET



Typical research questions (clinical / non-clinical)

# Discovery ADMET: means

- Primary **hepatocytes**, hepatocyte-like cells or transfected **cell lines**
  - suspension, (sandwich) culture, micro-fluidics based
- **Subcellular fractions** (microsomes, membrane vesicles)
- Dedicated ***In vitro* / *in silico* assay platform** for **drug induced cholestasis** (based on cell viability, confocal imaging and bile acid disposition)
- **Equilibrium dialysis** (and ultrafiltration) for determination of free fraction (fu)





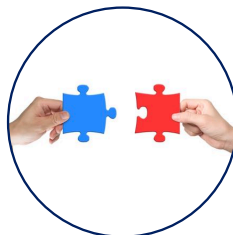
### 01/ PRAGMATISM

Sense of pragmatism leads to solutions for the most stormy projects.



### 03/ MORE THAN RESULTS

After reporting bioanalysis results, interpretation is supported by our multi-disciplinary team, allowing the customers to fly with the data.



### 02/ CONTEXT-OF-USE

Context-of-use method validations meet any fit-for-purpose budget.



### 04/ COMPLEMENTARY EXPERTISE

Apart from Bioanalysis, PMX and ADMET, our expertise comprises clinical pharmacology, formulation, ...

## BENEFITS FOR OUR CUSTOMERS



FAST - RELIABLE - HIGH QUALITY - SUSTAINABLE





### 05/ SYNERGY

The interplay between Bioanalysis, Pharmacometrics and ADMET within one company speeds up any program in a cost-effective way.



### 07/ ACTIONABLE INSIGHTS

Our PMX team turns data into actionable insights about your drug candidate.



### 06/ CONTINUOUS DIALOGUE

Regarding PMX projects, there is a continuous dialogue with experts of diverse background during the scoping, analysis, communication and decision making process.



### 08/ ACADEMIA & BIG PHARMA

Since our team has decades of experience in both Academia and Big Pharma, we flexibly adapt to the specific context of any customer.

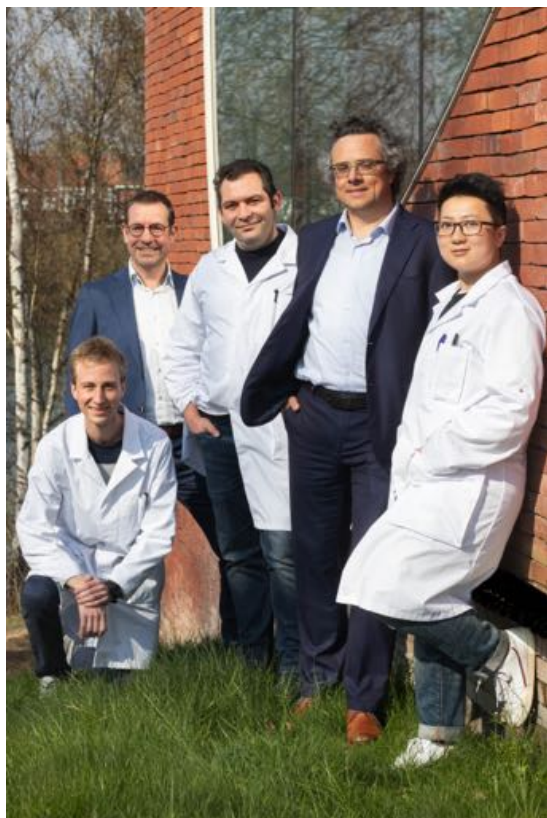
## BENEFITS FOR OUR CUSTOMERS



FAST - RELIABLE - HIGH QUALITY - SUSTAINABLE







## KEEP IN TOUCH WITH US

Please feel free to contact us by email or phone, if you require any further information.

**BioNotus<sup>®</sup>**  
BioAnalysis &  
Pharmacometrics

Siemon De Nys



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