An Overview of the Company and Our Services
RenaSci – Business Status

- Established in 2001 in BioCity, Nottingham
- CRO offering consultancy and specialised preclinical experimental services to the global pharmaceutical industry
- Key strength – *in vivo* pharmacology (90% of revenue)
- Part of the Sygnature Group since July 2018
- Complements the services of Sygnature Discovery which was founded in 2004 and is also based in BioCity, Nottingham
Sygnature Group Overview

- **Sygnature Discovery** provides high quality integrated or single discipline drug discovery support to pharma, biotech and not-for-profit organisations (from target validation to translational biology)
- Strong track record in drug discovery
  - 14 compounds delivered into the clinic (Phases I and II) since 2011
  - 13 compounds into pre-clinical development (excluding clinical compounds)
- 240 staff
  - 80% of scientists have PhDs
  - Considerable pharmaceutical industry R&D experience
- Private equity-backed company since September 2017
  - Senior management team are co-investors
  - Financially stable
  - Investment to fund expansion of capabilities & capacity

Peak Proteins - affiliated company provides protein production and crystallography

RenaSci - *In vivo* pharmacology expertise supports drug discovery & development
RenaSci – Overview

• We design, evaluate and validate biochemical and pharmacological techniques for use in drug discovery and development

• Experimental services focus on:
  − Abuse & Dependence
  − CNS
  − Obesity
  − Diabetes
  − NASH & Kidney Disease

• Key strength – *in vivo* studies including highly specialised animal models

• Consultancy offered on all aspects of drug discovery, preclinical and clinical development, regulatory approval, intellectual property protection and market positioning

• We have a successful track record in pharmaceutical R&D having assisted in taking >30 candidates into clinical development and 10 drugs to the market

• Our clients are from pharma, biotech, virtual companies and healthcare investors in UK, mainland Europe, Japan and USA

• We offer fee for service and FTE arrangements
RenaSci – Leadership

Executive Directors

Sharon Cheetham, PhD
Assistant Professor (Uni. Nottingham)

Rob Jones, PhD, MBA

David Heal, PhD, DSc
Visiting Professor (Uni. Bath)
Honorary Senior Lecturer (UCL)

Senior Vice President, Pharmacology

Steve Vickers, PhD
We work closely with our clients from study design through to study completion

- Experimental services tailored to meet specific requirements of each client including novel assay development if required
- State-of-the-art facilities
- Highly skilled and experienced team of over 30 scientists
- Data analysis by our fully-qualified statisticians
- Regular client updates from designated study director
- Flexible and responsive if studies change when in progress
- Agreed timelines
- Collection of samples for analysis by client or other CROs
  - For example, plasma and tissues for DMPK
- Necropsy and preparation of tissues for histology and immunohistochemistry
- Analysis of externally generated samples
- Data reporting from tabulated screening results to regulatory quality reports

Excellent reputation for reliability and high standard of work
Abuse and Dependence

Intravenous self-administration (IVSA)
- Wide range of reinforcers including stimulants, opioid agonists, nicotine and cannabinoid agonists
- Fixed and progressive ratio schedules
- ‘Break-point’ analysis to quantify the relative reinforcing effects of drugs

Drug discrimination
- Wide range of cues including stimulants, opioid agonists, dissociative anaesthetics, entactogens, hallucinogens and benzodiazepines

Tolerance and dependence
- 28 day on-dose/7 day withdrawal studies

Treatment of substance use disorders
- Use of procedures (eg IVSA) to assess novel treatments for substance use disorders including a rodent model of relapse to drug-seeking behaviour

Consultancy
- Study design and management
- Dossier preparation
- 8-factor analysis for drug scheduling
- Face-to-face meetings with FDA, DEA, EMA and other global agencies

ALTeC Abuse Liability Testing Collaboration
- Group of experts (RenaSci and Pinney Associates, USA) providing an integrated strategy for abuse liability testing in animals and man

Studies performed to GLP
CNS

**Ex vivo receptor binding**
- Novel assay development
- Biospace Beta-IMAGER™ technology for high-speed quantitative autoradiography

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**Microdialysis**
- Multiple neurotransmitters in one study
- Analysis of drug concentrations in microdialysates (by pharm-analyt)
- Simultaneous microdialysis, blood-sampling and behaviour (Culex Bambino/Raturn)

**Evaluation of antipsychotics**
- Conditioned Avoidance Responding
- Prepulse Inhibition
- Reversal of amphetamine, PCP or MK-801 locomotor activity and stereotypy
- Reversal of DOI-induced head twitch
- Catalepsy testing
- Antipsychotic-induced weight gain
- Plasma prolactin levels

**Rat model of binge-eating disorder**

**Models of compulsivity & impulsivity**

**Other assessments**
- Irwin profile and rotarod (safety assessment)
- Neurotransmitter-specific functional assays
- Seizure testing
- Brain neurochemistry
Obesity

In vitro/ex vivo assays
• Lipolysis in adipose tissue explants

Animal models
• DIO mice
• High fat fed ‘overweight’ rats
• DIO rats (cafeteria diet)
• Genetically obese animals
  – ob/ob and db/db mice, Zucker rats
• Drug-induced weight gain

Experimental measures
• Acute and chronic feeding studies
• Behavioural specificity
• Energy expenditure (metabolic profiling using the TSE PhenoMaster)
• Plasma analysis (OGTT/lipids)
• Collection and analysis of urine
• Faecal fat analysis
• Body composition analysis (chemical analysis, DEXA, FoodScan)
• Energy content by bomb calorimetry (faeces/carcasses)
• Cardiovascular measurements
• Inhibition of gastric emptying
Diabetes

Animal models
- Insulin resistance
  - Glucocorticoid-induced
  - DIO mice and rats
- Type 2 diabetes/diabetic complications
  - Genetically predisposed animals, for example, \(db/db\) mice, ZDF rats and ZSF1 rats
  - STZ-treated mice and rats on high fat diet

Experimental measures
- Glucose tolerance tests
- Plasma glucose, insulin, fructosamine
- HbA1c
- Plasma triglycerides, cholesterol, LDL-C, HDL-C, NEFA and leptin
- Urinary glucose excretion
- Pancreatic insulin content
- \(\beta\)-cell mass (performed out-of-house)
- Immunostaining for insulin and glucagon

Diabetic complications
- Diabetic neuropathy
  - Thermal pain sensitivity (Hargreaves test)
  - Mechanical allodynia (von Frey test)
- Diabetic nephropathy (see Kidney Disease)

In vitro techniques
- Perifused pancreatic islets
NASH & Kidney Disease

Gene expression analysis
• Collection of tissues to examine changes in gene expression of key markers associated with inflammation, fibrosis and steatosis

Animal models of NASH
• Mice fed methionine and choline deficient (MCD) or choline deficient (CD) diets (6 weeks)
• Normal and genetically obese mice fed high-fat, high-fructose, high-cholesterol diet (12 weeks)

Experimental measures – liver function
• Plasma parameters (ALT, AST, ALP, bilirubin, adiponectin HMW/total)
• Liver parameters (weight, triglyceride, cholesterol, NEFA, collagen)
• Liver histopathology (steatosis, lipid deposition, hepatic ballooning, lobular inflammation, NAFLD activity scores, fibrosis)

Animal models of kidney disease
• Adriamycin-induced nephropathy (mice)
• Diabetic nephropathy (genetic models of type 2 diabetes; STZ-treated mice and rats on high-fat diet)

Experimental measures – kidney function
• Plasma parameters (urea, creatinine)
• Urinary parameters (volume, albumin, creatinine, protein, albumin/creatinine and protein/creatinine ratios, the clinical biomarkers TIM-1 and cystatin-C)
• Glomerular filtration rate (FITC inulin clearance test)
• Kidney weight and histopathology (tubular protein, tubular degeneration/regeneration, tubulo-interstitial inflammation, glomerulosclerosis)
For further information:

www.renasci.co.uk
inform@renasci.co.uk