An Overview of the Company and Our Services
RenaSci - Business status

- Established in 2001
- Based in BioCity, Nottingham, UK
- Wholly owned by its Directors
- Independent company with no corporate financial liabilities
- CRO offering consultancy and specialised preclinical experimental services
- 90% of revenues generated from experimental services
RenaSci - Overview

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

• Experimental services focus on 4 key areas:
  − Abuse & Dependence
  − CNS
  − Obesity & NASH
  − Diabetes

• 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 operate fee for service and FTE arrangements

• RenaSci do not carry out internal research programmes
  − Avoiding any potential conflicts of interest
## RenaSci – Leadership

### Executive Directors

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<thead>
<tr>
<th>Name</th>
<th>Position and Affiliations</th>
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<tr>
<td>Sharon Cheetham, PhD</td>
<td>Assistant Professor (Uni. Nottingham)</td>
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<td>Rob Jones, PhD, MBA</td>
<td>Company Secretary (Contracts)</td>
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<td>David Heal, PhD, DSc</td>
<td>Visiting Professor (Uni. Bath)</td>
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<td></td>
<td>Honorary Senior Lecturer (UCL)</td>
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### Senior Vice President, Pharmacology

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<th>Name</th>
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<tr>
<td>Steve Vickers, PhD</td>
<td>Senior Vice President, Pharmacology</td>
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RenaSci - Experimental services

At RenaSci 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 qualified and experienced team of 33 scientists
• Data analysis by our fully-qualified statisticians
• Further personnel delivering a range of additional roles and supporting functions
  – Administration, financial, business development, occupational health
• Regular client updates from designated study director
• Flexible and responsive if studies change when in progress
• Agreed timelines
• Data reporting from tabulated screening results to regulatory quality reports
• Analysis of externally generated samples
• 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
Abuse & 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

**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

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

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
- NASH and fibrosis

Experimental measures
- Acute and chronic feeding studies
- Behavioural specificity
- Energy expenditure (CLAMS)
- 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
- Liver lipids/enzymes/collagen content/pathology

In vitro/ex vivo assays
- Lipolysis in adipose tissue explants
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
  - Adriamycin-induced nephropathy (CKD)

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

Experimental measures - diabetic complications
- Plasma markers of renal failure/hepatotoxicity
- Urinary albumin excretion, creatinine, total protein
- Glomerular filtration rate
- Kidney weight and histopathology
- Diabetic neuropathy

In vitro techniques
- Perifused pancreatic islets