Institution: University of Sheffield

Unit of Assessment: 1 - Clinical Medicine

a. Context

Sheffield University's Medical School generates societal impact from rigorous, broad-based preclinical studies, translational and experimental research. Our impact stories change clinical practice, generate wealth and most importantly improve the lives of patients. Impact delivery is fostered by an innovative infrastructure. This includes the Healthcare Gateway, the NIHR Sheffield Clinical Research Facility, the Experimental Cancer Medicines Centre, a Clinical Trials Unit and the Joint Clinical Research Office. Local, national and international interactions facilitate development of our impacts. For example, collaborators include the local NHS, School of Health and Related Research, Dental School, and the Faculties of Science and Engineering. Extensive external interactions with academic partners are complemented by collaborative R&D projects with UK and overseas industry.

Main non-academic beneficiaries of the unit's research: Impact from the unit changes the lives of patients, informs regulatory policy, and affects medical health professionals in the UK and worldwide. The impact of our research is also seen in economic benefits to the pharmaceutical and medical device sectors, the public purse and commerce. The general public, patients and user-groups benefit from our impact through public engagement activities.

Main types of impact specifically relevant to the unit's research: The impacts we have achieved span the entire translational spectrum and reflect the range of research activities carried out within the School. Relevant types of impact are listed below followed by examples:

Health and welfare impacts

- Aclasta/Reclast, an effective treatment for osteoporosis, clinical trials led in Sheffield, licensed in over 100 countries with over 2 million doses administered since 2007*****
- Brilinta/ticagrelor for myocardial infarction (MI), licensed in 2010/11 (EU/USA)*****
- Safer treatment of childhood leukaemia through improved delivery of thiopurine drugs*

Economic impacts

- Changed radiological practice with new imaging technology that won 2011 Medical Futures Award for Best Translational Research for Respiratory Innovation
- Our spinout companies won investment, grants and license income totalling over £9M*

Production impacts

- Spin-out Diurnal pioneered a drug therapy for Congenital Adrenal Hyperplasia*****

Public engagement

- Our staff interact with several lay advisory panels e.g. Bone Research, HIV, Cancer Research
- The Sheffield Motor Neurone Disorders Research Advisory Group (SMND RAG) brings together those affected by MND to inform research and has close interactions with SITraN

Practitioners and services

- The WHO FRAX® tool, developed in collaboration with Sheffield, used to assess fracture risk in over 6.8M patients worldwide (01/06/2011-7/11/13) is endorsed by NICE CG146*

Public policy

- Review of the Organ Donor Register (Report to Secretary of State, 2010)
- Published 42 clinical/diagnostic guidance articles since 1/1/08 cited over 1900 times
- Effective treatment for tens of thousands of patients requiring emergency anticoagulation*

Commerce

- 27 UK and 28 overseas companies have funded R&D worth £8.7M since 01/01/2008
- Diurnal Ltd raised £4M investment and took Chronocort to Phase 2 clinical trials*
- Our spin-out company **SimCyp Ltd** was sold Certara for $32,000,000 in 2012*****

***** *Indicates impact case study submitted.*

b. Approach to impact

Methodology for translating research into impact:

Identification of potential impact: A Commercial Assessment System (CAS) is embedded into the grant application process. Staff consider whether their research could generate exploitable IP, services or software at the time of project costing. Staff complete an online form which is directed to staff in the Sheffield Healthcare Gateway (SHG) *via* the university's Research and Innovation Services (RIS) who provide access to IP professionals and consultants. The SHG evolved from the Sheffield Medical Innovation Centre founded within the School, a HEIF 4 funded initiative in 2008. SHG provides KE support to the School and wider university (see details below).

Funding the Pathway to Impact: A total of 23 HEIF-funded proof-of-concept (PoC) schemes (£580k) have been initiated since 2008. In addition, the Faculty was awarded Wellcome ISSF (2011) and £400k MRC CinC grants (2012), both of which provide funding to bridge the "valley of death". Awards were in the range of £10-50k and have helped leverage further development funding e.g. Azzouz received £10k in 2010 for a PoC study in spinal muscular atrophy therapy that resulted in a DPFS award of over £600k in 2011. Other ongoing/recent impact-facilitating awards include: The MRCT supported development of "Natural transglutaminase inhibitors for use in kidney transplantation" (Johnson, £130k) which led to a patent filing (PCT/GB2013/051373) and MRC DPFS funding of £490k; Testing and development of devices for predicting pre-term birth (Anumba) supported by MRC DPFS and NIHR I4I funding (total value £940k); The IL-A HEART Study, an MRC Experimental Medicine Award (Crossman *et al.* £745k). Gunn and Hose (UOA12) won BHF and Wellcome Trust Health Innovation Challenge Fund awards to develop software for aiding therapeutic decisions in ischaemic heart disease (>£1M, in total).

Collaboration with industry: We hold 2 MRC AstraZeneca Mechanisms of Disease initiative awards. Renshaw was recently awarded the first-ever MRC Industry Fellowship Partnership Award (with GSK) for disease models for drug discovery. Collaborative R&D income from our spin-outs *vide infra*, often initially funded via FusionIP and White Rose Seedcorn funding, proved to be an important facilitator of impact delivery (R&D contracts of over £900k to TUOS since 2008). Pre-clinical development of gene therapy for Parkinson's disease (collaboration with Oxford BioMedica Ltd) attracted significant recognition in 2012 (funding of over £5M, including an ERC Advanced Fellowship worth £2.1M for Azzouz). Collaborative R&D funding from 27 UK and 28 overseas companies amounted to £8.7M, providing further evidence of the School's active translational partnerships.

Encouraging Entrepreneurship & Spin-outs: The Medical School's staff have been encouraged to start up spinouts where appropriate for some time e.g. Adjuvantix (2000), Asterion (2000), Simcyp (2001, case study A1-2), Molecular Skin Care (2002), Diurnal (2004, case study A1-6), Medella Therapeutics (2007), and PH Therapeutics (2013). FusionIP Ltd partners with TUOS to exploit its R&D activities, facilitating access to the White Rose Technology Seedcorn Fund, Local Development Association (LDA) grants, MRC DPFS and BBSRC Follow-on Funding schemes and the private sector to support these early stage spin-outs. The difficult financial climate for raising venture capital that prevailed in recent years led us to adapt a flexible approach over the current assessment period in which partnering and licensing (R&D agreements with external agencies) has become the predominant mode of engagement with industry and other users.

Developing and Sustaining Relationships with User Groups: We have developed projects of mutual interest with companies such as AstraZeneca (case study A1-5), Novartis, Pfizer and others as well as not for profit organisations including the Sheffield Teaching Hospital Foundation Trust (STH), Dementias and Neurodegenerative Disease Research Network, Cancer Research UK, the Social Care Institute for Excellence and the DoH, Leukaemia & Lymphoma Research and the MRCT. Interactions with external users are also promoted by the Sheffield Healthcare Gateway and facilitated e.g. the Pfizer Strategic Agreement (in 2010). Under the Agreement, a Strategy Executive with membership from UoS, Pfizer as well as the STH (Pfizer funding to School PIs exceeds £700k) facilitates collaboration. End users are involved in many aspects of translational research through Consumer Panels in cancer treatment programmes e.g. in piloting the BresDex decision laboratory. The Sheffield Cancer Research Centre engages with end users and fundraisers via open days and lab visits (over 200 people) and members of the North Trent Consumer Research Panel sit on our governance committees. The WHO FRAX® tool has been used to assess over 6.8M patients worldwide (01/06/2011-7/11/13, case study A1-3) and was

developed through collaboration with the World Health Organization. Our researchers engage with the both CRUK and the British Heart Foundation via regular open days for their Fundraisers and by regular media interviews, thereby raising awareness of the prevention, pathology and treatment of cancer and cardiovascular disease respectively. Storey is on the steering committees for a number of pharma companies developing new anti-platelet treatments e.g. AstraZeneca. He has received KE and PoC funding from TUOS (case study A1-5).

Our MR imaging groups and Medical Physics provide examples of a long-term engagement with GE Healthcare and Philips respectively, interactions that are facilitated by funding from The Wellcome Trust, DoH, and EU to deliver impact in the neonatal imaging, diagnostics and cardiovascular medicine. For example, Wild developed new MR imaging technology (POLARIS) that won the *2011 Medical Futures Award for Best Translational Research for Respiratory Innovation* in collaboration with the STH (Kiely, CatC) and was originally supported by EPSRC and EU funding and is now used in routine clinical diagnosis in the UK.

We have encouraged our staff to interact with agencies such as the European Medicines Agency to seek Orphan Drug Status (ODS) and since 2008 have obtained ODS in areas such as: the treatment of ACTH dependent Cushing's Syndrome (Newell-Price, EU/3/10/798 OD/038/10, c.a. 24,000 patients in the EU); treatment of Spinal Muscular Atrophy (Azzouz, EU/11/876 OD/169/10, c.a. 15,000 patients in the EU); and treatment of Amyotrophic Lateral Sclerosis (Shaw, EU/3/12/954 OD/106/11, c.a. 40,000 patients in the EU). Securing ODS is a step on the pathway to impact for new therapies in rare diseases (see case study A1-6).

How we support staff to achieve impact: The National Institute for Health Research Sheffield Clinical Research Facility and Clinical Research Office are partnerships between the Sheffield Teaching Hospitals NHS Foundation Trust and University of Sheffield. They provide comprehensive assistance to researchers conducting clinical research by working closely with our colleagues in the NIHR Research Design Service for Yorkshire and the Humber, the University of Sheffield Clinical Trials Research Unit and the NIHR Sheffield Clinical Research Facility (CRF), a streamlined service that supports stimulation, development, set-up, costing, and management of clinical research in Sheffield. Since its establishment, the CRF has supported over 300 studies, recruited 10,936 new patients (pre-screened 22,632) and achieved or surpassed recruitment targets on 48 studies in year.The Sheffield Healthcare Gateway provides KE support to the Medical School and has become a centre for the faculty. It evolved from the Sheffield Medical Innovation Centre founded within the School, a HEIF 4 funded initiative in 2008. SHG uses a bottom up approach to developing impact, with business managers working at the bench with clinicians and scientists to leverage support through seedcorn, proof of concept, and translational funds to deliver key milestones and move ideas along the translational pathway. The SHG has the remit to support and stimulate academic engagement with industry. SHG and RIS provide regular targeted updates of funding opportunities and arrange for user groups to attend showcase days at which selected researchers present translational projects to e.g. GSK, Novartis, Pfizer, CRUK, MRCT, CRT.

Early career researcher training via the Think Ahead Program (developed within the School) includes modules on Innovation, Enterprise & Industry, networking and non-academic career paths. It also runs the Industrial Knowledge Forge (InKForge) to develop links with industry, and instils KE in early career researchers through industrial networking and partnering for research projects. Since its launch in 2012, 41 industrial visitors from companies including GSK, Lonza, AstraZeneca, Lilly, Unilever, Novartis, Metaphase, Peakdale Molecular, Tissue Gnostics, Allergan, OI Pharma and Kymab Ltd have taken part in 22 events. Seminars and workshops were attended by on average 15-20 ECRs per event.

Incentives for KE: Recognition of translational research performance is instilled in University strategy and recognised in annual staff appraisals at departmental level. Achievement of impact is a major factor in promotions at all academic levels. Individuals have been awarded bonuses for exceptional or sustained impact activities. We offer our spin-out founders equity stakes of 40% in their companies. TUOS staff retain at least 60% net income share on sales of patents to a FusionIP company and 30-50% of all net income generated from licensing revenues. School staff are encouraged to apply for patents when suitable IP is identified, e.g. 38 US patent applications were filed by School staff and 8 US patents were granted since 01/10/08. Generous consultancy arrangements whereby staff retain the first £5,000 of gross consultancy income after which a

12.5% overhead is charged on all income received.

c. Strategy and plans

Our Impact, Innovation and Knowledge exchange strategy sets out the key priorities that the University adopts to maximise the impact of its research. The strategy has 4 key strands:

To create and maintain deeper partnerships with external organisations; To engage with the Sheffield city region; To make the most of intellectual property; To embed impact, innovation and knowledge exchange in the organisation. This overarching policy has been adapted locally to the needs of our unit and guides the SHG and InKForge schemes to empower our staff to deliver on this strategy and generate impact. Over the next 5 years we will:

Expand partnerships for Impact: Our researchers will grow their network of external partners and make the most of the intellectual property generated by our research, aided by SHG and by our strategic partnership with FusionIP for developing impact. The University's commercialisation team with SHG are active in promoting to academics the benefits of developing an IP portfolio that could potentially benefit the University or the local or national economy. Proof of concept funding will be used to add value to our IP.

Exploit: The National Institute for Health Research Sheffield Clinical Research Facility and Clinical Research Office to deliver effective clinical trials and facilitate the evaluation of new medicines. As well as promoting translational research with external partners, it will promote links with STH academic directorates. Our SHG business managers will work alongside clinicians and scientists to leverage support through seedcorn, proof of concept and translational funds to deliver key milestones and move ideas along the translational pathway. SHG will help us access innovation funding from a range of sources (e.g. DPFS, MRCT, TSB, industry). It will organise regular events to showcase our projects to industry executives.

Develop new spin outs and licensing opportunities: FusionIP Ltd will help us achieve impact through licensing and spin-out development and has raised a further £20M fund in 2013 for investment into University spin-outs. Sheffield spin-out companies ranked third in the UK (after Oxford University and Imperial College London spin-outs) in 2012 in securing external equity investment totalling £10M. In 2012, the SHG led on a successful bid to obtain £400k MRC Confidence in Concept award to TUOS, monies that are now supporting 10 early-stage translational healthcare projects. A further application for £450k was made in Sept. 2013.

Reinforce a KE culture: KE Champions and mentors will be introduced into departments to raise "pathway to impact" awareness and recognition of commercial opportunities.

d. Relationship to case studies

We have submitted the following case studies to exemplify the impacts of our research:

A1-1. **A new gold standard treatment for the emergency correction of warfarin-induced coagulopathy**

A1-2. **Commercial and health impacts of drug modelling tools** (SimCyp Ltd)

A1-3. **FRAX, an international tool for the assessment of fracture risk**

A1-4. **Health and economic impact of a new drug intervention for osteoporosis** (Aclasta/Reclast)

A1-5. **New drug for heart attack victims** (Ticagrelor for MI)

A1-6. **Clinical development and manufacture of a new drug, Chronocort®, for treatment of the rare orphan disease congenital adrenal hyperplasia** (Diurnal Ltd)

A1-7. **Safer treatment of childhood leukaemia through improved delivery of thiopurine drugs**

A1-2 and A1-6 are examples of our strategy to encourage staff to set up spin-outs. A1-6 also involved staff seeking EMA orphan drug approval. A1-4 and A1-5 describe impact deriving from clinical trials and collaborations between clinical academics with expertise in their respective fields that synergized with industry (AstraZeneca and Novartis, respectively). A1-4 also involved local collaboration with the Sheffield School of Health and Related Research. A1-3 is the result of a collaboration between the World Health Organisation and our experts in osteoporosis. A1-7 involved the work of pharmacologists in our unit collaborating with the haematologists from the Sheffield Children's Hospital and Barts and the London Hospital. A1-1 involved an experimental medicine approach carried out with groups in Aberdeen and Cambridge.