Institution: University of Strathclyde		
Unit of Assessment: B8 - Chemistry		
Title of case study: Creating enhanced capabilities in drug discovery research with GSK		
Period when the underpinning research was undertaken: 2000-2015		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Prof William Kerr	Professor	01/10/1989 – present
Prof John Murphy	Professor	01/09/1995 – present
Prof Tell Tuttle	Professor	01/01/2007 – present
Prof Nick Tomkinson	Professor	01/06/2011 – present
Prof Glenn Burley	Professor	01/04/2011 – present
Dr Craig Jamieson	Reader	09/08/2010 – present
Period when the claimed impact occurred: August 2013 - 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact

A unique collaborative programme was devised to provide GlaxoSmithKline (GSK) employees in drug discovery with emerging scientific knowledge and access to alternative research methods based on the expertise of Strathclyde researchers. The initiative has had distinct impact on GSK's scientific operations, the productivity and creativity of its researchers (26 patents; >95 GSK authored papers; >100 prizes), and the externally recognised reputation of the company (through multiple industry awards). GSK has further invested substantially in expanding the programme to include non-GSK personnel, which has now also benefitted other companies in the wider Healthcare sector. Since August 2013, 115 employee and non-employee participants have been engaged in the overall programme.

2. Underpinning research

The impact is primarily founded on research outputs by Kerr and Murphy in aspects of synthetic methods and catalysis of direct relevance to medicinal chemistry. From 2000 to 2009, senior personnel at GSK became increasingly aware of and engaged with the distinct and sustained contributions from these chemists, which led to the initiation of the collaborative programmes that have generated the impact described. Subsequent recruitment of Burley, Jamieson, Tomkinson and Tuttle to the Chemistry staff at Strathclyde augmented the programme and expanded the range of contributing expertise in the areas of synthesis, catalysis, medicinal chemistry, chemical biology, and computational and theoretical chemistry.

Kerr's and Murphy's novel research in synthesis and catalysis, including extensive collaborations with GSK (14 co-authored publications with GSK in 2000-2009), led to significant advances relating directly to both bench and process scale pharmaceutical endeavours. Kerr developed a series of key synthetic methods and asymmetric processes [**R1**] with new organometallic reagents for application throughout preparative chemistry, and catalysts with direct relevance to the pharmaceutical industry. Murphy's prominent outputs regarding a suite of super electron donors were deemed pivotal studies in the area [**R2**], providing a highly creative contribution to reactivity in organic synthesis. Such developments allowed the innovative use of neutral organic molecules as powerful, yet tuneable, reagents in sustainable, metal-free, reduction processes.

Since 2009, Strathclyde has strengthened the research base of the relationship with GSK by adding the expertise of Burley in nano-assembly, diagnostics and biomedicine [**R3**], and Jamieson and Tomkinson in medicinal chemistry and chemical biology [**R4**, **R5**]. Specifically, Burley's pioneering concepts in the area of selective recognition of unique and biologically relevant DNA sequences, Jamieson's design of novel lead and clinical candidate compounds in the

neurosciences area, and Tomkinson's interrogation of the function of orphan nuclear receptors, represent key examples recognised by GSK as leading outputs in areas that strongly overlapped with their internal business portfolio and overall ambitions. Furthermore, the industry-based research alignment with GSK and Strathclyde was enhanced substantially by Tuttle in the field of computational and theoretical chemistry. Tuttle's theoretical focus on biochemical systems informed development of compounds with anti-cancer properties, as well as the ability to accurately describe binding interactions in biochemical systems using computational methods [**R6**].

The consistent production of research outputs from the Strathclyde team in areas of interest to GSK provided the underpinning drivers to establish a significant and expansive research and training partnership with Strathclyde. This is explicitly stated by the Director of UK Chemistry Recruitment & Talent Development, GSK: '*Inspired by existing research collaborations and recognising the quality and direct relevance of the research outputs of the associated team of Strathclyde academics, GSK approached Strathclyde with the objective of formulating a distinct collaborative research platform…'* [**S1**].

The advances in preparative and medicinal chemistry together with the innovative approaches devised by the Strathclyde researchers have underpinned and grown a unique, award-winning collaboration with GSK that has positively impacted the company's drug discovery programmes, the staff involved and the wider healthcare sector, well beyond that expected at the onset of the relationship.

3. References to the research (Strathclyde affiliated authors in **bold**; FWCI at 02/02/2021)

R1 **Henderson, K. W.**, **Kerr, W. J.**, and **Moir, J. H.** (2000) Enantioselective Deprotonation Reactions Using a Novel Homochiral Magnesium Amide Base, Chem. Commun., 479-480. DOI: 10.1039/B000425L. [FWCI: 2.24]

R2 **Murphy, J. A.**, **Khan, T. A.**, **Zhou, S. -Z.**, **Thomson, D. W.**, and **Mahesh, M.** (2005) Highly Efficient Reduction of Unactivated Aryl and Alkyl Iodides by a Ground-State Neutral Organic Electron Donor, Angew. Chem. Int. Ed., 44: 1356-1360. DOI: 10.1002/anie.200462038. [FWCI: 1.49]

R3 **Krpetic, Z.**, **Singh, I.**, Su, W., **Guerrini, L.**, **Faulds, K.**, **Burley, G. A.**, **Graham, D.** (2012) Directed Assembly of DNA-Functionalized Gold Nanoparticles Using Pyrrole-Imidazole Polyamides, J. Am. Chem. Soc., 134*:* 8356-8359. DOI: 10.1021/ja3014924. [FWCI: 1.52; REF2 in 2014]

R4 **Caldwell, N.**, Harms, J. E., Partin, K. M., **Jamieson, C.** (2015) Rational Design of a Novel AMPA Receptor Modulator through a Hybridization Approach, ACS Med. Chem. Lett., 6: 392-396. DOI: 10.1021/ml5004553. [FWCI: 0.64]

R5 Trump, R. P., **Bresciani, S.**, Cooper, A. W. J., **Tellam, J. P.**, **Wojno, J.**, Blaikley, J., Orband-Miller, L. A., Kashatus, J. A., Boudjelal, M., Dawson, H. C., Loudon, A., Ray, D., Grant, D., Farrow, S. N., Willson, T. M., **Tomkinson, N. C. O.** (2013) Optimized Chemical Probes for REV-ERBα, J. Med. Chem., 56: 4729-4737. DOI: 10.1021/jm400458q. [FWCI: 1.12]

R6 **Frederix, P. W. J. M.**, **Ulijn, R. V.**, **Hunt, N. T.**, and **Tuttle, T.** (2011) Virtual Screening for Dipeptide Aggregation: Toward Predictive Tools for Peptide Self-Assembly, J. Phys. Chem. Lett., 2: 2380-2384. DOI: 10.1021/jz2010573. [FWCI: 1.59; REF2 in 2014]

Notes on the quality of research: All referenced outputs were peer-reviewed ahead of publication. The body of underpinning research was supported by the following grants:

I. Kerr. EPSRC (01/09/2005-31/01/2009). New Magnesium-based Enantioselective Deprotonation Methods: Greener General Base Strategies and the Development of a Catalytic Protocol. Total Awarded: GBP205,288.

II. Murphy. EPSRC (01/10/2006-30/09/2009). New Horizons in Organic Electron Transfer. Total Awarded: GBP374,415.

III. Burley. EPSRC (01/04/2012-31/3/2013). New Molecular Tools for the 21st Century: Molecular Design of New DNA-based Devices. Total Awarded: GBP922,000.
IV. Tomkinson. EPSRC (01/07/2011-31/12/2014). Innovative Targets for Circadian Drug Discovery: REV-ERBα and RORα. Total Awarded: GBP1,210,241.
V. Tuttle. EPSRC (19/09/2008-18/09/2011). Applications and Development Methodologies for Designing Hybrid Catalysts. Total Awarded: GBP273,319.

4. Details of the impact

Establishment of a Partnership between Strathclyde and GSK

The partnership with GSK was initiated in 2009 due to a distinct desire by the company to enhance the professional development and research-aligned capabilities of its drug discovery scientists as part of a sustained mission of continuous improvement. It was GSK's intention to establish a unique research and training platform which *'… would (i) provide GSK Chemists with an environment of continuous professional development that would equip them to achieve greater levels of scientific excellence, and (ii) enhance our scientific execution through direct collaboration'* [**S1**]. The influence of the Strathclyde chemists in achieving GSK's objectives was realised initially through GSK employees registering as Strathclyde MPhil/PhD students, and undertaking work-based research projects, with both GSK Industry and Strathclyde Academic supervision.

As the programme became established, senior GSK personnel commended the initiative for opening new pathways to research escalation, knowledge exchange, and staff advancement, noting that it was delivering business benefits well beyond the original aims [**S2**, page 1]. As the Senior Vice-President and Chief Chemist, GSK, commented [**S3**]: *'This programme has led to enhanced levels of project-relevant scientific knowledge, advanced thinking, and overall scientific rigour … The established collaborative framework has had a positive impact on and is now contributing extensively to overall organisational learning within GSK.*'

Buoyed by early successes of the scheme, GSK extended the collaborative programme with Strathclyde by additionally funding non-employee graduates to enrol as Strathclyde PhD students situated in GSK's laboratories. Since August 2013, 115 employee and non-employee postgraduate researchers have been engaged directly in GSK-aligned discovery and development projects, with 79 students having graduated so far with higher degree awards (72 PhD and 7 MPhil) [**S1**]. The collaborative programme is recognised within GSK as a landmark initiative for the development of early talent and is central to GSK's strategy and policy. The direct funding committed to the programme by GSK, to date, has exceeded GBP7,700,000, reflecting the commitment of the approach across GSK. The success of the expanded scheme has resulted in a range of benefits to GSK and the wider UK and international healthcare sector:

- Enhanced the translation of innovative research approaches and methodologies into industry.
- Improved the performance, productivity, rigour and creativity of the researchers involved.
- Furthered GSK's reputation, and associated GSK with distinct positive advancements in the pharmaceutical industry.
- Contributed to a highly skilled workforce in the wider healthcare sector.

Impact on GSK's Scientific Operations and Innovation

The core impact has been on GSK's operational practices and culture, and the influence this has had on specific projects in medicinal chemistry, chemical biology and process chemistry leading towards the discovery and development of new transformational medicines. The Strathclyde – GSK strategic relationship has enhanced the translation of new science into industry, allowing distinctive and ambitious initiatives to be more readily adopted [**S1**].

In synthesis, preparative routes to previously less accessible molecular structures have been opened and new more sustainable bench and process-aligned methods established. In addition, advanced computational methods are guiding the understanding of biochemical systems within

several drug discovery programmes. Projects have focussed on various diseases, including respiratory and inflammatory diseases, tuberculosis, and malaria. To date, 5 chemical entities associated with the Strathclyde partnership are progressing in GSK's drug discovery pipeline with clinical trials targeted [**S1**], 26 patents filed, and >95 GSK co-authored papers published [**S4**].

Impact on GSK Staff, Standards of Training, and CPD

The scheme has led to enhanced researcher performance, productivity, rigour, and creativity from the scientists involved, as well as within the wider chemistry teams [**S2**, **S3**]. To date, 50 GSK *employees* have benefitted from the continuous professional development programme and it is notable that 4 of the 5 newly appointed senior team leaders at GSK in 2015 were *employee* graduates of the PhD programme, with three others similarly promoted in 2016/17 [**S1**]. Further to this, 11 *non-employee* scientists who graduated from the programme have now been appointed to leadership roles in permanent positions within GSK.

A further benefit has been a notable culture shift with regards to engagement of GSK scientists with the wider scientific community. In addition to a five-fold increase in scientific literature publications [**S1**], GSK employees have contributed significantly to the over 100 national and international awards/prizes received by participants on the programme to date, which have included the *2015 Royal Society of Chemistry Young Industrialist of the Year,* the *2017 Salters' Centenary Award,* the *Society of Chemical Industry Young Chemist in Industry (2015, 2016, 2017, and 2020),* and the *Society of Chemical Industry Scholarship Award (2018, 2019, 2020)*. Additionally, since the start of the programme there has been a doubling of candidates receiving GSK *Exceptional Science Awards* further reflecting the impact of the framework's training excellence [**S1**].

Impact on GSK's Reputation

Following significant accolades from the Scottish and UK Governments pre-2013 [**S5**, **S6**], the programme has been highlighted as a case study of excellence in reports by Universities UK [**S7**, page 39] (2014) and the Association of the British Pharmaceutical Industry [**S8**, page 3] (2016). External awards received for the programme include winner of *Best Business Partner* category at the *Prospects Postgraduate Awards* (2013); the *Excellence in Skills* award at the *Cogent Life Science Skills Awards* (2014); the *Best Commercial Programme* at the *Training Journal Awards* (2014); and the *Skills Award* from the *Chemical Industries Association* (2017). One of the most significant accolades to date, has been the *2019 Princess Royal Training Award* to GSK, with the Strathclyde programmes at the core of this award submission [**S1**].

Furthermore, the philosophy adopted through the collaborative programmes is consistent with evolving thought-leadership within the pharma industry (e.g. Schultz and Campeau, *Nature Chemistry*, **2020**, *12*, 661-664), demonstrating that GSK is at the forefront of approaches to improve the efficiency and effectiveness of industrially based drug discovery and culture. The programmes have also had a positive and tangible impact on GSK's reputation as an employer as evidenced by the 100% increase in applications to the company's 2014 recruitment campaign in comparison to that held a few years earlier [**S1**]. GSK's enhanced reputation as an employer has been further exemplified by *GSK Chemistry* receiving the *Learning and Development Award* at the 2020 *Personnel Today Awards*.

Impact on the Wider Healthcare Sector

In addition to *non-employee* participants transitioning to permanent employment with GSK, several graduates from the programme have progressed to UK and international postdoctoral roles, with the remainder achieving competitively won positions within a broad array of national and international pharmaceutical organisations, such as AstraZeneca, Heptares, Charles River, Astex, Cancer Research UK, Evotec, Pharmaron, and Reckitt Benckiser. These individuals are having a significant influence on R&D programmes within these companies [**S9**, **S10**]. The Head of Chemistry and DMPK, Charles River Laboratories reports:

> *'… we are now reaping the benefits with a number of alumni now part of our company, including our Associate Director of Chemistry. … these colleagues are now delivering notably elevated levels of impact within our laboratories … [they] have, on several occasions, overcome significant synthetic chemistry challenges to deliver appreciably complex molecules for our client drug discovery programmes. Additionally, [they] have also contributed to the design of novel drug-like molecules, actively and strategically embedding their developed new skills, such as computational modelling, in order to do so. … I firmly believe that the established Strathclyde-GSK higher degree programmes … are delivering tangible impact across the sector.'* [S9]

In summary, this initiative represents a synergistic and fresh approach that elevates the impact of academia-industry partnerships to a new level, developing and delivering a highly skilled cadre of industry-ready scientists. Complementary expertise from each partner has maximised innovation and research performance at GSK, which is catalysing the generation of new and essential healthcare products, has influenced the culture and creativity of individual scientists and collaborative teams, and extensively raised training standards, all leading to broader benefits to the wider healthcare sector with eventual downstream positive impacts on public health.

5. Sources to corroborate the impact

S1 Corroborating statement from Director, UK Chemistry Recruitment & Talent Development, GSK, dated 31 July 2020.

S2 GSK-University of Strathclyde Collaborative PhD Programme 2009-2016 Report, with Foreword from then President GSK Pharmaceuticals R&D, now Chief Scientific Adviser to the UK Government.

S3 Corroborating statement from Senior Vice President and Chief Chemist, GSK, dated 31 July 2020.

S4 For a full list of publications based on research carried out as part of the collaborative projects, please see: https://www.strath.ac.uk/science/chemistry/strathclydegsk/ourpublications/

S5 Scottish Parliamentary Motion, Life Sciences Cross Party Group (13/01/2010). https://bit.ly/3d30iBB

S6 Sir Tim Wilson's Review of University-Business Collaboration commissioned by the UK Government, Chapter 5, Section 5.9.2, Pages 62-63 (28/02/2012). https://bit.ly/399Xfqm

S7 Universities UK (UUK) and the UK Commission for Employment and Skills (UKCES) report, Forging Futures: Building Higher Level Skills through University and Employer Collaboration, Case Study 12, p.39 (22/09/2014). https://bit.ly/3cTbrF2

S8 Association of the British Pharmaceutical Industry report, Developing Talent and Partnerships to Create New Medicines, ABPI (September 2016). https://bit.ly/2QnhtpV

S9 Corroborating statement from Head of Chemistry and DMPK, Charles River Laboratories, dated 31 July 2020.

S10 Corroborating statement from Director of Medicinal Chemistry, Pharmaron, dated 31 July 2020.