Institution: University of Dundee		
Unit of Assessment: UoA5 Biological Sciences		
Title of case study: Exscientia Ltd, a rapidly-growing market leader in Artificial Intelligence (AI)-driven drug discovery, saving time and costs for global Pharma		
Period when the underpinning research was undertaken: 2008-2012		
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 Andrew Hopkins	Professor of Medicinal Informatics	2007- 2020
Period when the claimed impact occurred:		
Is this case study continued from a case study submitted in 2014? Y/N		

1. Summary of the impact

Exscientia, a spin-out company of the University of Dundee created by Prof Andrew Hopkins FRSE, has grown into a market leader in artificial intelligence drug design technology. Since 2014, the company has attracted GBP84 million investment, earned revenue of GBP23.9 million, created 88 highly-skilled jobs, and serviced 18 partnerships with major global Pharma and others (GBP538 million in disclosed deals, with more undisclosed). Exscientia has reduced the time and cost of pre-clinical drug discovery and has delivered two novel drugs into first-in-human clinical trials, being the fastest AI-design drug company to reach that critical stage.

2. Underpinning research

The world has rarely been more acutely aware than it is now of the time and cost involved in the development of new drugs and vaccines. The pharmaceutical Industry is facing serious pressures, given estimates of a USD2.6 billion cost and 10-15 year timeline for developing a new drug. Declining drug discovery R&D productivity is the most important challenge to address. One approach to tackle this problem is to harness chemical, pharmacological and biological data for automated drug design. **Prof Andrew Hopkins** has been at the forefront of this research by combining machine learning and big data analytics to tackle questions of target identification, polypharmacology and *de novo* compound design.

Hopkins is a pioneer of 'network pharmacology', coining the phrase in 2007 and expanding in a seminal 2008 review cited 1,324 times **[R1]**. Network pharmacology combines biological network analysis with chemical biology approaches, to design new drugs to perturb biological networks rather than individual targets. This is contrary to conventional drug discovery approaches based on highly specific targeting of a single protein that often lead to lower than desired clinical efficacy. Network pharmacology is the concept that drugs for many diseases may require multiple activities to be most effective. This research by Hopkins opened up a new subfield in drug discovery **[R1]**.

The creation of ChEMBL in 2008, provided the first publicly-available database of bioactive molecules including pharmacological and chemical structural-activity relationship data that, significantly, was in a format amenable to reading by computers. Taking advantage of this resource, Hopkins embarked on a research project to harness the high-quality chemoinformatics data and apply machine-led learning to the process of new drug design. His team systematically integrated data derived from different disciplines including computational modelling **[R2]**, synthetic chemistry, biophysics **[R3]**, pharmacological testing and clinical studies, to develop methods and algorithms **[R4, R5]** to automate drug design. Hopkins collaborated with experimentalists at the University to efficiently design novel patentable chemicals for synthesis

and then test the compounds designed by the algorithms **[R2]**. This resulted in creation of an automated, adaptive methodology for designing drug ligands to multi-target profiles, with a 75% prediction success rate verified experimentally and the predicted target engagement confirmed *in vivo* **[R2-R6]**.

It was quickly realised that the computational technology platform developed by the University of Dundee offered a highly scalable system to generate intellectual property **[R5,R6]**. Spin-out Exscientia Ltd was created in 2012 as a technology platform company aiming to revolutionise productivity in drug discovery using data analytics and AI (Artificial Intelligence) techniques of machine learning during the initial phases from chemical design to production of a clinical candidate.

3. References to the research

[R1] Hopkins, AL (2008) 'Network pharmacology: the next paradigm in drug discovery', *Nature Chemical Biology*, vol. 4, no. 11, pp. 682-690. DOI: 10.1038/nchembio.118
This paper is the highest cited paper ever published in *Nature Chemical Biology* since 2008.

[R2] Besnard, J, **Ruda, GF**, Setola, V, **Abecassis, K**, Rodriguiz, RM, Huang, X-P, **Norval, S**, Sassano, MF, Shin, AI, **Webster, LA**, **Simeons, FRC**, **Stojanovski, L**, Prat, A, Seidah, NG, Constam, DB, **Bickerton, GR, Read, KD**, Wetsel, WC, **Gilbert, IH**, Roth, BL & **Hopkins, AL** (2012) 'Automated design of ligands to polypharmacological profiles', *Nature*, vol. 492, no. 7428, pp. 215-220. DOI: 10.1038/nature11691 This paper received significant coverage, with News and Views features in *Nature Reviews Drug Discovery* and *C&E News* and in the press (including the BBC https://bbc.in/3e5K0Ks)

[R3] Navratilova, **I** & **Hopkins, AL** (2010) 'Fragment Screening by Surface Plasmon Resonance', *ACS Medicinal Chemistry Letters*, vol. 1, no. 1, pp. 44-48. DOI: 10.1021/ml900002k

[R4] Bickerton, GR, Paolini, GV, **Besnard, J**, Muresan, S & **Hopkins, AL** (2012) 'Quantifying the chemical beauty of drugs', *Nature Chemistry*, vol. 4, no. 2, pp. 90-98.
DOI: 10.1038/NCHEM.1243

[R5] Patent: **Besnard, Jeremy** and **Hopkins, Andrew Lee**. (2011) *Design of Molecules.* World Intellectual Property Organization Patent no. PCT/GB2010/051940 (WO2011061548). Available at https://bit.ly/2Oi2YTK

[R6] Patent: **Besnard, Jeremy**, **Hopkins Andrew Lee, Gilbert, Ian**, Ruda Gian Filippo, Abecassis, Keren (2012) *Morpholino compounds, uses and methods.* World Intellectual Property Organization Patent no. PCT/GB2012/051194 (WO2012160392) Available at https://bit.ly/3qu0EGp

Key research grants relevant to this case study:

1. **Hopkins, AL** Exscientia: Commercialising Multi-Target Drug Design. BBSRC Follow on Fund (2011- 2012). Value: GBP150,100
2. **Hopkins, AL** Experimental Proof of Concept for Drug Design Selective Optimisation Algorithm. BBSRC Pathfinder Award for Drug Design Proof-of-Concept (2009-2010). Value GBP13,759

4. Details of the impact

a) Raising multi-million investment in, and revenue from, AI-guided drug design
Exscientia has rapidly-grown into a leading pharmatech company at the forefront of AI drug discovery. Since 2017, Exscientia has raised a total of GBP84 million, comprising:

- Series A EUR15 million in 2017 **[E1]**
- Series B USD26 million in 2019 **[E2]**

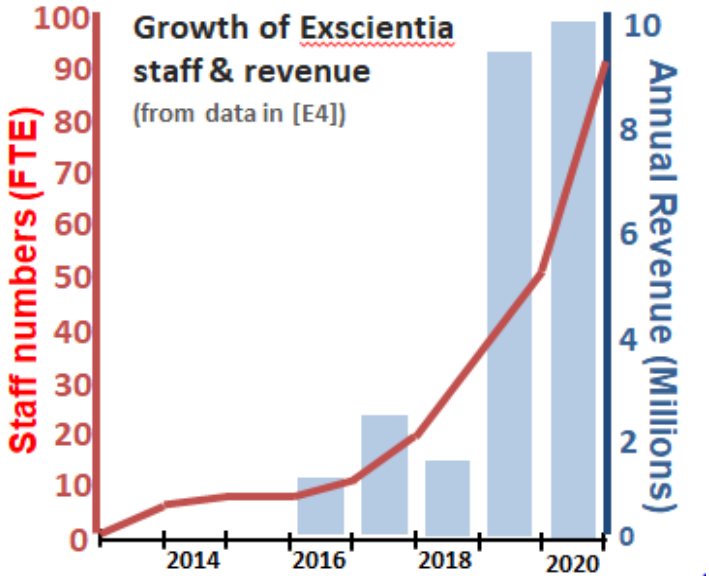
- Series C USD70 million in 2020 **[E3]**

(including USD10 million raised after the announcement).

Evotec, one of four investors, said of Series A in 2017:

> "*Our investment in Exscientia represents Evotec's single biggest equity placement to date and in, what we feel, is the world leading AI technology company*" **[E1]**.

Exscientia's revenue rose from GBP1.5 million in 2018 to GBP9.8 million in 2020, with GBP23.0 million total revenue since 2016 **[E4]**. This enabled Exscientia to expand from its initial space in Dundee, to a second office in Oxford (2017), then into larger premises on the Oxford Science Park (2018). Recently (2019/2020), offices opened in Osaka (Japan) and Miami (USA). In the REF period, expansion increased the workforce from 3 to 91 staff **[E4]** by creating 88 highly-skilled new jobs (headcount: 88; FTEs: 88) with staff numbers doubling each year for the past 3 years (Figure).



b) Innovation and partnership with Pharma to accelerate drug discovery using AI

In addition to its own pipeline, Exscientia provides services to pharmaceutical companies where its automated AI drug design process can accelerate development of candidates for clinical trial.

These services have attracted 18 partnerships on 28 separate projects, developing drugs or technology for a range of diseases, including cancer, COVID-19, psychiatric disease, bone disease, fibrosis and others **[E4]**. Many collaborations are with global Pharma companies with revenue generated through initial upfront and research payments, near-term and clinical milestone payments, and royalties on final products. Examples of such deals include: Bayer (2019; EUR240 million), Roche (2019; CHF67 million), Celgene/Bristol Myers Squibb (2019; USD25 million upfront, with undisclosed milestones), GlaxoSmithKline (2017; GBP33 million), Sanofi (2017, EUR250 million), Sunovion (2014; total USD4.8 million) **[E4]**. Partnerships also exist with GT Apeiron, Evotec, SRI, RallyBio, Blue Oak, Huadong Medicine, IMI CARE, Diamond Light Source/Calibr, Sumitomo Dainippon Pharma, and the Gates Foundation **[E4]**. Twelve patents were filed or published on Exscientia molecules/methods in the REF period **[E4]**.

c) Significant efficiency and cost savings compared to conventional drug discovery

Published industry benchmarks estimate it takes 4.5 years and USD63 million to get to pre-clinical testing of a drug candidate. In 2014, Exscientia signed a partnership with Sumitomo Dainippon Pharma Ltd and one year later delivered a molecule meeting Sumitomo criteria **[E5]**. Fewer than 400 compounds needed to be synthesized to identify the final compound using

Exscientia's automated system, saving over 80% costs in these drug discovery stages, or 30% of the total drug development cost **[E4, E6]**. The Director of Sumitomo's chemistry team said:

> "*Working with Exscientia has been transformative, enabling us to progress projects far faster than had previously been possible*", and their Director of Drug Development added, "... *projects by ex scientia are providing exciting productivity and efficiency gains…"* **[E5]**.

In 2019, Exscientia provided GlaxoSmithKline with a first selective, potent *in vivo*, lead molecule, discovered in 5 iterative cycles with only 85 compounds tested **[E7]** in comparison with industry benchmarks of 2,500 per project. Also in 2019, Sanofi exercised its option to advance a compound from their 2017 partnership where Exscientia designed bispecific-binding molecules after triaging >1,000 disease-relevant target combinations and designing nearly 100 billion novel compounds. The first-in-class bispecific molecule being progressed by Sanofi interacts with two drug targets related to inflammation and fibrosis - normally needing two separate drugs **[E8]**.

These achievements highlight the efficiency and productivity gains made possible through Exscientia's algorithms. Their current pipeline has 12 drug discovery projects **[E4],** and 5 new drug candidates have been delivered in under 14 months, far quicker than the 4.5 to 5-year industry benchmark and with associated cost savings **[E7]**. Evotec confirm:

> "*Through our partnership with Exscientia we have seen first-hand evidence that they can deliver the most productive drug discovery engine in the industry*" **[E2]**.

d) Fastest AI-designed drugs to accelerated IP filing and first-in-human clinical trials
Exscientia has been the fastest AI-design drug developer in the world to reach the clinic, enabling accelerated IP filing. In January 2020, though partnership with Sumitomo Dainippon Pharma Ltd, Exscientia delivered into Phase 1 clinical trials the first AI-designed drug ever to be tested in humans **[E9].** The drug, in trial in Japan, treats patients with obsessive-compulsive disorder, enabling Sumitomo to expand its pipeline to treat key unmet needs in psychiatry/neurology. Sumitomo's Senior Executive Officer said:

> "*We are very excited with the results of the joint research that resulted in the development of candidate compounds in a very short time…*" **[E9]**.

An Exscientia-proprietary AI-designed drug targeting cancer is also in Phase I first-in-human clinical trial, enrolling its first participant in December 2020 **[E9]**. Exscientia and Hopkins have received numerous accolades (collated in **E10**) and their leading position in the sector is confirmed by many:

> GSK say "*Exscientia has… proven innovation in drug discovery technologies…their industry-leading approach will accelerate the discovery of new molecules"* **[E4]**;
>
> Forbes list Exscientia as a "*leading AI drug discovery startup*" for possible acquisition by Big Pharma for over USD2 billion in the near future **[E10]**;
>
> Evotec say "[Exscientia's] *AI approaches…can positively and radically impact drug discovery"* **[E1]**.

5. Sources to corroborate the impact

[E1] Press Release on Investment by Evotec. Financial Times, 'Exscientia announces investment from Evotec'. *Frontier IP Group PLC*. 28th September 2017.

[E2] Press Release on Series B funding round and Roche partnership. Financial Times, 'Exscientia Series B funding & Roche collaboration' *Frontier IP Group PLC*. 7th January 2019.

[E3] Series C funding announcement, 'Novo Holdings leads USD60m Series C financing round in Exscientia'. *Novo Holdings.* 26th May 2020.

[E4] Corroboratory testimonial statement from Exscientia and collated partnership deal press releases.

[E5] Exscientia statement on partnership with Sumitomo Dainippon Pharma 2015, 'Exscientia Ltd, reaches first delivery milestone in collaboration with Sumitomo Dainippon Pharma Co., Ltd'. *Exscientia* 2nd September 2015. Available at https://bit.ly/37vvc4l

[E6] Exscientia featured in Deloitte Insights report. Deloitte Insights 2019, 'Intelligent drug discovery' *Deloitte.com* pp21-23. 7th November 2019 Available at https://bit.ly/3mxplj0

[E7] Press release on delivery of preclinical candidate for GSK. Financial Times, 'Exscientia reaches first major milestone with GSK'. *Frontier IP Group PLC*. 4th April 2019

[E8] Press release on product development and license option agreement with Sanofi. Exscientia, 'Sanofi Exercises option on Exscientia-designed bispecific small molecule for treatment of immunological conditions' *Exscientia.ai* 5th August 2019.

[E9] (i) Financial Times article on first AI designed drug to enter human clinical trials. Murgia M 2020 'AI-designed drug to enter human clinical trial for first time'. *Financial Times.* 30th January 2020. Available at https://on.ft.com/2KfBDzp; and Press Release 2020, 'Exscientia: world first trials of new drug candidate created by artificial intelligence' *Frontier IP Group plc.* 31st January 2020. Available at https://bit.ly/3paWaDE

(ii) Phase 1 Clinical Trial of Exscientia drug EXS21546. Sponsor: Exscientia 2020, '3-part Study to Assess Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of EXS21546' *ClinicalTrials.gov (NCT04727138).* 8th December 2020. Available at https://bit.ly/3a4LTol

[E10] Compilation of external accolades and awards.

(i) 2015 BBSRC Commercial Innovator of the Year
(ii) 2015 Scottish Enterprise award for Life Sciences Entrepreneurial Business Leadership
(iii) 2017 OBN Awards Best Emerging Biotech Company
(iv) 2017 RSC Chemistry World Entrepreneur of the Year
(v) 2019 Lifestar Awards Series B Finance Raise of the Year
(vi) 2019 Top 20 most promising world companies using AI drug discovery (American Chemical Society Discovery Report page 13)
(vii) 2020 Sunday Times Tech Track 100 league table
(viii) 2020 OBN Awards Best Established Biotech company finalist
(ix) Condie B & Dayton L 2020, 'Four AI technologies that could change the way we live and work' *Nature.com* 9th December 2020. Available at https://bit.ly/37r6dyS
(x) Toews R 2020, '10 AI Predictions for 2021' *Forbes* 22 December 2020. Available at https://www.forbes.com/sites/robtoews/2020/12/22/10-ai-predictions-for-2021/?sh=4c45ab05d1a0