Institution: University of Oxford

Unit of Assessment: 8 - Chemistry

Title of case study: OMass Therapeutics: New technology for drug discovery with economic benefit to the UK

Period when the underpinning research was undertaken: 2013 - 2018

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:
Professor Dame Carol Robinson	Dr Lee's Professor of Chemistry	2009 – present
Dr. Jonathan Hopper	Postdoctoral Researcher	29/11/2011 – 31/03/2016
Dr. Hsin-Yung Yen	Postdoctoral Researcher	02/06/2014 – 31/03/2016
Dr. Arthur Laganowsky	Postdoctoral Researcher	01/07/2011 – 30/06/2014

Period when the claimed impact occurred: April 2016 – 31 July 2020

Is this case study continued from a case study submitted in 2014? No

1. Summary of the impact (indicative maximum 100 words)

OMass Therapeutics is a fledgling drug discovery company focused on developing treatments for rare immunological and genetic diseases with high unmet patient need. At its core is patented mass spectrometry technology, developed in Professor Robinson's laboratory at the University of Oxford, which enables rapid identification of small molecules that modulate membrane protein assemblies associated with disease. In the four years since its inception, the company has:

- Underpinned the development of new technology for drug discovery
- Generated over GBP40,000,000 of investment
- Created over 30 highly-skilled jobs
- Boosted the UK and local economies through expansion of its facilities and high-value, specialised mass spectrometers.

2. Underpinning research (indicative maximum 500 words)

Understanding how small molecules bind to membrane proteins is critical to many drug discovery programmes. However, the difficulties inherent in studying such interactions for membrane proteins have long been recognised. Various biophysical methods exist but in most cases are inefficient because they require large quantities of modified membrane proteins, rely on secondary or indirect outputs, or are not amenable to high-throughput screening.

The technology developed in Robinson's laboratory at the University of Oxford uses novel mass spectrometry methods to measure binding to unlabelled membrane protein targets directly through a change in mass. It is able to uncover actual binding interactions and inform function on a rapid timescale, with minimal sample consumption and with unlabelled proteins.

The research underpinning this technology began in 2013 when Robinson first demonstrated that intact, folded, membrane proteins could be propelled into the gas phase with therapeutic agents remaining in place [**R1**]. This unexpected finding had significant potential since membrane proteins represent around 50% of key drug targets worldwide. These data were used to file her first patent granted in 2017 in Europe and the US (Detection of membrane protein-therapeutic agent complexes by mass spectrometry) [**R2**].

At that stage (2013) the approach was poised for further development with respect to understanding the physical processes involved in the ionisation of membrane proteins and the

effects of binding to therapeutics. In 2014, Robinson found that membrane protein complexes also retained many lipid molecules that would be key to undertanding their function [**R3**]**.** This research was highlighted on the front cover of the journal *Nature.* Robinson developed this further to show the consequences of lipid and drug binding to membrane-embedded complexes.

Simultaneously, Robinson was developing and refining instrumentation to assist in her research, in particular, the desorption electrospray ionisation (DESI) platform [**R4**] for membrane proteins, which won an Innovate UK award from the UK Government in 2017. In 2016 the research had been advanced to the point of commercial application and OMass Technologies, a spin-out company from the University of Oxford was established.

In 2017 Robinson's research team at the University of Oxford determined the mass spectrometry conditions that enabled a folded G-protein coupled receptor (GPCR) to be released into the gas phase with its small molecule therapeutic intact [**R5**]. Since GPCRs are the target of at least 30% of all current drugs this was a major step forward. Robinson went on to show how mass spectrometry could be further developed to demonstrate how agonists and antagonists could modulate the signalling of these receptors critical to drug discovery [**R6**].

3. References to the research (indicative maximum of six references)

R1. Journal article: J. Marcoux, S. Wang, A. Politis, E. Reading, J. Ma, P. Biggin, M. Zhou, H.Tao, Q. Zhang, G. Chang, N. Morgner and C. V. Robinson. Mass spectrometry reveals synergistic effects of nucleotides, lipids and drugs binding to a multidrug resistance efflux pump. Proc. Natl. Acad. Sci. USA, 2013, DOI: 10.1073/pnas.1303888110. Citations: 136 (Google Scholar 02/12/2020)
R2. Patent No. US9536718B2: https://patents.google.com/patent/US9536718B2/en
Granted 2017; describes detection of membrane protein-therapeutic agent complexes by mass spectrometry
R3. Journal article: A. Laganowsky, E. Reading, T. M. Allison, M. B. Ulmschneider, M. T. Degiacomi, A. J. Baldwin and C. V. Robinson. Membrane proteins bind lipids selectively to modulate their structure and function. Nature, 2014, DOI: 10.1038/nature13419. Citations: 517 (Google Scholar 02/12/2020)
R4. Journal article: S. Ambrose, N. G. Housden, K. Gupta, J. Fan, P. White, H-Y Yen, J. Marcoux, C. Kleanthous, J. T. S. Hopper and C. V. Robinson. Native desorption electrospray ionization liberates soluble and membrane protein complexes from surfaces.
Angew Chem Int Ed Engl, 2017, DOI: 10.1002/anie.201704849. Citations: 25 (Google Scholar 02/12/2020).
R5. Journal article: H. Y. Yen, J. T. S. Hopper, I. Liko, T. M. Allison, Y. Zhu, D. Wang, M. Stegmann, S. Mohammed, B. Wu and C. V. Robinson. Ligand binding to a G protein-coupled receptor captured in a mass spectrometer. Science Advances, 2017, DOI: 10.1126/sciadv.1701016. Citations: 31 (Google Scholar 02/12/2020)
R6. Journal article: H-Y Yen, K. K. Hoi, I. Liko, G. Hedger, M. R. Horrell, W. Song, D. Wu, P. Heine, T. Warne, Y. Lee, B. Carpenter, A. Plückthun, C. G. Tate, M. S. P. Sansom and C. V. Robinson. PtdIns(4,5)P2 stabilizes active states of GPCRs and enhances selectivity of G-protein coupling. Nature, 2018**,** DOI: 10.1038/s41586-018-0325-6. Citations: 95 (Google Scholar 02/12/2020)

4. Details of the impact (indicative maximum 750 words)

Pathways to Impact: From Research to Commerce

Creation of service company to inform drug discovery
OMass Technologies, a spin-out from Professor Robinson's laboratory, was established in 2016 with GBP1,100,000 investment primarily from Oxford Sciences Innovation. The company was set up to provide a service to pharmaceutical R&D by identifying key lipids and other cofactors bound to proteins of interest – information which could then be used to further their own in-house drug development.

The company was founded based on a portfolio of patents, including one to discover therapeutic agents, which protect the mass spectrometry platform developed in Professor Robinson's laboratory [**R2**]**.** The patented technology was licensed by an agreement between OMass and Oxford University Innovation (OUI), the University's Intellectual Property Office. **[Text removed for publication]** [**E1**].

The patented technology enabled the rapid identification of small molecules that modulate membrane protein assemblies associated with disease, and OMass attracted a client base of 9 pharmaceutical and biotechnology companies actively researching membrane protein therapeutic targets. **[Text removed for publication]** Access to Robinson's technology allowed an unprecedented level of insight into critical membrane protein targets, particularly their lipid binding properties **[text removed for publication]**.

More informed characterisation of therapeutic targets also led to more rapid expedition of drug discovery pipelines for OMass' client base [**E2**]**.** After the first full year of trading OMass had a staff of 3.5 FTE [**E4**] and an annual turnover of GBP287,603 [**E3**].

Impacts

Award-winning technology

In parallel with developing its service offering, OMass applied to the Open Round Competition held by Innovate UK, the UK's innovation agency. Funded by the UK Government, Innovate UK drives productivity and economic growth through support to develop new, innovative ideas. The submission, entitled 'A new platform for drug discovery on membrane protein targets', was successful and in June 2017 OMass received GBP481,722 to develop its prototype drug discovery platform into an essential technology to interface with mass spectrometers (award no. 103843). This enabled high-throughput characterisation of how drugs bind to membrane-embedded protein targets.

External investment

The increasing demand from industry for their unique technology could no longer be handled effectively with the existing team, so in 2017 Robinson sought investment to enable OMass Technologies to expand. Specifically, she wanted to increase the number of full-time employees and also acquire further bespoke mass spectrometers and laboratory space to expand the existing service company. Robinson had already identified a preferred investor – Syncona, a FTSE250 company focused on founding, building and funding global leaders in the Life Sciences.

In summer 2017, approximately a year after OMass' inception, Robinson made her first pitch for investment. Syncona immediately recognised the potential of the platform and the value of the information OMass was generating for the pharmaceutical industry [**E4**]. Instead of investing in the existing company, partners at Syncona convinced Robinson and the OMass team to establish a drug discovery pipeline that would retain key information about membrane protein targets in-house – essentially creating a drug discovery company.

Since drug development is a lengthy and expensive process with a high attrition rate, long-term investment is critically important yet often difficult to secure. Syncona's strategy is to fund right through to commercialisation, a process which can take up to 15 years and GBP100,000,000s – such investor confidence is critical for a drug discovery company where candidate development is a long-term and challenging process. Securing investment from Syncona was a breakthrough: of some 200 pitches, Syncona typically makes investments in 0 to 3 companies per year **[text removed for publication]** [**E4**]. OMass was now included in this highly competitive group.

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Creation of drug discovery company

In 2018, two years after its foundation and with venture capital of GBP14,000,000, OMass Technologies relaunched as OMass Therapeutics, a drug discovery company in its own right. The

new company focused on understanding its targets at the molecular level and developing treatments for a range of rare immunological and genetic diseases with high unmet patient need [**E7, E9**]. With expanded series A investment of GBP27,500,000, led by Syncona, larger than any Series A UK biotech funding round in 2019, a total of GBP41,500,000 has been invested in the 2-year old drug discovery company [**E8**].

Creation of highly-skilled employment opportunities

From the original 3.5 FTE staff after the first year of trading, by July 2020 OMass had a head count of 32 FTEs [**E9**]. Drug discovery encompasses different scientific disciplines and the posts created within the company are highly skilled (27 of the 32 employees hold PhDs) and include chemists, computational scientists, strategists, pharmacologists, structural biologists and biochemists. Scientists occupying these positions come from a diverse range of countries including the UK, Germany, France, Taiwan, Albania, Greece, Brazil, India, Venezuela and Australia. Senior management has been recruited from the US (CEO, previously President and Chief Business Officer of Bicycle Therapeutics) and the UK pharmaceutical industry (Chief Scientific Officer and Vice Presidents of Medicinal Chemistry, Finance and Strategy recruited from senior positions in Heptares and GSK, respectively) [**E10**].

Acquisition of UK spin-out company

In 2018 OMass realised that to inform its therapeutic targets fully it needed to include cell-based assays to complement the biophysical mass spectrometry measurements. Accordingly, a collaboration with Excellerate (a spin-out company of the University of Nottingham) was initiated, with OMass providing funding for 2 FTEs. Within a year OMass realised the importance of this complementary information and moved to secure this expertise in-house by acquiring Excellerate and its 8 FTEs, ensuring sole rights to their cell-based assays for OMass target proteins. OMass Nottingham is now integrated with OMass Oxford. In addition to acquiring a skillset of 8 highly-trained pharmacologists, the former Chief Scientific Officer of Excellerate has been appointed to the OMass Executive Leadership team [**E11**].

Contribution to local and wider UK economy

OMass Therapeutics is currently valued at GBP49,500,000 based on the last round of financing (2020) [**E4**]. The company occupies purpose-built open plan laboratories and offices in the Schrodinger Building in The Oxford Science Park. Its sister company, OMass Nottingham, occupies laboratories and office space at BioCity Nottingham, the re-generated former Boots R&D Centre. Both facilities are important contributors to the local Oxford and Nottingham economies. Additionally, the company has made significant contributions to the UK and local economies through the purchase of instrumentation (more than GBP1,500,000) and other laboratory equipment (approximately GBP750,000) as well as through the outsourcing of services to UK companies to carry out its activities. The latter includes engagement of external consultants and expanding the OMass chemical library (now 170,000 compounds) to support its screening programmes.

Today, OMass Therapeutics has four main drug discovery programmes that utilise Professor Robinson's technology. From a rare neurodevelopmental disorder, to inflammatory bowel disease that affects some 7,000,000 patients world-wide, all indications have in-life health consequences [**E9**]. After just over 4 years, the research, technology and know-how developed in Robinson's laboratory at the University of Oxford have been harnessed to form a viable drug discovery company, crucially focused on unmet patient need – a company which, after only two years of trading, is already contributing significantly to the UK economy in terms of new technology, jobs, facilities investment and purchasing power.

5. Sources to corroborate the impact (indicative maximum of 10 references)

E1. Letter from Oxford University Innovation (OUI) detailing licence agreements, including values, between OUI and OMass.
E2. [Text removed for publication]

E3. Accounts: OMass Therapeutics (formerly OMass Technologies) accounts for a small company made up to 31st December 2018 (Companies House). Turnover figure for 2017 is on page 7.
E4. Letter from Syncona (FTSE250 Life Sciences Investor) giving detail of investment in OMass, rationale for investment, and impact of Professor Robinson's work.
E5. Journal article: *D. Chorev et al, Protein assemblies ejected directly from native membranes yield complexes for mass spectrometry, Science, 2018, 362, 6416, 829-834.* This paper details a radical new way of releasing membrane proteins into the gas phase – patent application filed and subsequently licensed to OMass – (OMass licensed albeit not yet granted).
E6. Journal article: *L. Urner et al, Modular detergents tailor the purification and structural analysis of membrane proteins including G-protein coupled receptors, Nature Communications, 2020, 564.* This paper details detergent conditions for the analysis of GPCRs – patent application filed and subsequently licensed to OMass – (OMass licensed albeit not yet granted).
E7. OMass Therapeutics website (https://omass.com) detailing the objectives and science of the company.
E8. Press release detailing extended Series A finance for OMass Therapeutics (17/02/2020)
E9. Letter from Chief Executive Officer of OMass Therapeutics detailing impact of company, current portfolio and rationale for taking up position.
E10. OMass website showing key personnel in OMass team (short biographies)
E11. Press release detailing OMass acquisition of Nottingham University spin-out Excellerate Biosciences (25/02/2020)