

MRC Translational Research 2008-2018

Evaluation Report: Analysis of Spin-Outs (Annex A2.7)





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Annex A2.7 Translational Research: Spin-Outs

This Annex provides an overview of the economic impacts of the MRC's awards for translational research over the last ten years, focusing on the spin-outs established by Principal Investigators to exploit the intellectual property developed. The analysis is based on a database of spin-outs derived from self-reported accounts compiled from Researchfish¹ and other sources of intelligence gathered by the MRC. This database has been linked to records of the performance of those companies in securing capital to progress the commercialisation of their underlying intellectual property. The Annex concludes with an analysis focused on the degree to which these commercialisation outcomes can be attributed directly to the awards made by the MRC.

1.1 Spin-outs emerging from the MRC's translational research awards

The data compiled for this paper showed that:

- A total of 134 spin-outs were attributed by Principal Investigators to the MRC's awards for research funding that were incorporated between 2008 and 2017 (covering those emerging from the directed and non-directed translational research portfolios and those spin-outs attributed to other awards made by the MRC). 124 of these companies remained active in 2019. A further 18 spin-outs were reported that were incorporated in 2018 or 2019, though as there are substantial reporting lags in the Researchfish records, the following analysis is restricted to those companies incorporated by the end of 2017.
- 123 of these companies were established in the UK. The remaining 11 were established in the US (6), Switzerland (2), Finland, Germany and Canada (1 each).
- The numbers of spin-outs established rose steadily over the period, peaking in 2016. The drop-off observed in 2017 and 2018 could be explained by recording lags. This has some support from the interviews with PIs, which highlighted several companies emerging from the grant portfolio that had only been established comparatively recently and do not yet appear in MRC records.
- Forty four percent of the spin-outs (60 of 134) reported emerged from Oxford, Cambridge, KCL, UCL, and Imperial College.



2012

Year

Number of Spin-outs

2013

2014

2015

2016

2017

Figure 1.1: Number of spin-outs attributed to MRC translational research grants awarded since 2008, by year of incorporation

Source: MRC spin-out database, Companies House

2009

2010

2011

0

2008

¹ Researchfish, March 2019.

1.1.2 Distribution of spin-outs by translational grouping

The following table illustrates the distribution of spin-outs by the broad 'translational grouping' of the relevant award made by the MRC (note that multiple grants may be associated with the same spin-out). Fifty-eight percent of the 134 spin-outs were associated with an award made through the directed translational research portfolio (and 51 percent with awards made through the focused translational grouping). Twenty-seven percent emerged from the non-directed translational research portfolio, while 17 percent emerged solely from other awards made by the MRC.



Figure 1.2: Share of spin-outs attributed to MRC funded research, by translation grouping

Source: MRC spin-out database, Pitchbook. Note that one spin-out could be attributed to multiple awards and may appear in multiple portfolios.

1.1.3 Spin-outs in context

Putting this in context, figures from the Office for Life Science Medical and Biopharmaceutical Database indicate that of 6,340 companies active in the biotechnology and medical technology sectors in 2017, 1,982 were incorporated since 2008. 55² of these were spin-outs attributed to MRC translational research funding). On an illustrative basis, this indicates that three to seven percent of new enterprises formed in the sector since 2008 have emerged from MRC funding³.

There were marked differences in the profile of spin-outs emerging from MRC funding and other active start-ups founded since 2008. Almost half of spin-outs attributed to MRC research were operating in the core 'biopharma' sector (defined as manufacturers and developers of advanced therapies, antibodies, blood and tissue products, small molecules, therapeutic proteins, and vaccines), relative to 17 percent in the wider sector. Advanced therapy developers were particularly overrepresented (14 percent of spin-outs attributed to MRC research versus 3 percent in the industry more widely). Most other segments were underrepresented in the portfolio of spin-outs attributed to MRC research – and most significantly digital health (1 percent versus 13 percent in the industry more widely).

² While the OLS Medical and Biopharmaceutical Database is the best available register of firms active in the life science industries, it is not complete and numerous spin-outs from MRC funded research are not captured in the database. ³ I.e. 55 to 134 as a share of 1,982.



Figure 1.3: Activities of spin-outs attributed to MRC funded research and activities of all active companies incorporated in the biopharma and medical technology sectors since 2008

MRC spin-outs Companies in biopharma and medical technology sector founded since 2008

Source: MRC spin-out database, OLS Biopharma and Medical Technology Database. Table based on sample of 55 spin-outs attributable to MRC funded research captured with the OLS database.

1.2 Equity investment

Records of the spin-outs attributed to MRC funded research were linked to records of investment activity captured by Pitchbook to provide metrics of the success of those companies in attracting capital to progress their activities. Pitchbook compiles and structures information on disclosed venture capital and private equity investments as well as exits (in the form of IPOs and acquisitions), drawing on information in regulatory filings, press releases, and websites. Pitchbook was used as a key source of data for HM Treasury's Patient Capital Review. While the data is close to complete for significant fundraisings, there are gaps in coverage for smaller or undisclosed investments (such as those made by angel networks or if companies are operating in 'stealth mode'). The following passages should be reviewed with this caveat in mind.

1.2.1 Equity investment in spin-outs

In terms of the investment raised by spin-outs:

- Overall, 54 of the 134 spin-outs (40 percent) emerging from MRC funded research attracted external equity investment by the end of August 2019⁴. A total of £1.3bn was raised in external equity funding over a total of 150 funding rounds⁵. Ninety-three percent of this capital was raised by spin-outs based in the UK.
- The bulk of this capital (£962.6m) was raised over 143 private funding rounds (i.e. angel investments or venture capital). Four spin-outs progressed to raising funding from capital markets through IPOs or private investments in public equity, raising a further £382.6m, discussed in more detail below.
- It is challenging to break these figures down by the five groupings for translational research, as many spin-outs were based on research produced over multiple grants. Those 'backed' by multiple grants were more likely to

⁴ This only includes those deals where the value of the investment made was disclosed. A further 16 companies had obtained external funding, grants or participated in accelerator programmes where the value of any external investment was unknown.
⁵ Including angel investment, crowdfunding, venture capital, convertible debt, and IPOs and fundraising in capital markets, but excluding any control transactions via private equity or corporate buy-outs.

raise equity finance, so the figures below will overstate the share of spin-outs raising external finance. However, it does indicate that spin-outs attributed to awards made through the directed translational research portfolio were more likely to raised capital, and raise funding in greater amounts, than non-directed approaches.





Source: MRC spin-out database, Pitchbook. Note that one spin-out could be attributed to multiple awards and may appear in multiple portfolios.

Fundraising was overwhelming concentrated amongst spin-outs located in London, Cambridge, Oxford and Stevenage as illustrated in the figure below. This mirrors wider patterns of concentration of venture capital investment in the UK, but also reflects that investors have recently shown substantial appetite for investment in advanced therapies and most spin-outs focused on this modality have emerged from UCL. However, this does raise questions as to how effective commercialisation efforts may be in the long-run amongst companies based outside these hubs (and the interviews with PIs highlighted an example where the founders were forced to relocate from Nottingham to Cambridge to forge links with investors).

Figure 1.5: Total fundraising by headquarter location of spin-outs attributed to MRC funding, by August 19



Source: MRC spin-out database, Pitchbook, UK headquartered firms only. Private and public transactions

1.2.2 Wider sector context

Figures were also extracted from Pitchbook to set the figures presented above in the context of overall fundraising activity of firms active in relevant sectors⁶ that were incorporated over the same period (i.e. were founded from 2008 onwards):

- A total of 713 firms founded between 2008 and 2018 raised external equity investment by August 2019. Using figures from the OLS Biopharma and Medical Technology database as an approximation of the total number of start-ups in the relevant sectors, this gives an illustrative estimate that around 36 percent of firms in the wider sector secured external investment.
- These firms raised a total of £5.1bn in external equity investment over the period, across 1,591 funding rounds. Around 70 percent of this was raised by firms active in the biotechnology and drug discovery industries. Of the top 20 largest funding rounds over the period by value, 12 were launched by advanced therapy developers (including Orchard, Nightstar, MeiraGTx, Freeline Therapeutics, Adaptimmune and Autolus⁷), and a further five by developers of other types of therapeutics (Kymab, Mereo Biopharma, Mission Therapeutics, and Artios). The remaining three were launched by CMR Surgical (a developer of surgical robots), Babylon Health (developer of GP at Hand) and Clinigen (a general pharmaceutical and health services firm). The largest deal of the period was a £442m private investment in Babylon in August 2019, valuing the company at £1.6bn.
- Spin-outs attributed to MRC funded translational accounted for around 24 percent of all equity investment in startups in the sector founded between 2008 and 2018. This contribution has risen with time, reaching 21 percent in 2017 and 41 percent in 2018, as illustrated in the following figure.
- Spin-outs attributed to MRC funded research appear more likely to attract equity funding, and attract funding in larger amounts, than other start-ups in relevant sectors. This may be product of differences in the profile of the two groups of companies firms in the medical technology sector are likely to have less intensive capital requirements than those following a drug discovery pathway. There was, however, little evidence that spin-outs faced constraints or barriers in attracting external funding relative to other start-ups in the sector.





Source: Pitchbook, UK headquartered firms only

 ⁶ Pharmaceuticals and Biotechnology, Healthcare Devices and Supplies, Healthcare Technology Systems and Digital Health.
 ⁷ All of these companies are connected to MRC funding. Orchard, Nightstar, Freeline and MeiraGTx have been attributed the awards in the scope of the study. However, Autolus and Adaptimmune were attributed to older MRC grants

1.2.3 Investors

The spin-outs attributed to MRC funded research attracted capital from 211 different investors in private funding rounds that made a total of 425 investments⁸, including 89 venture capital and/or private equity funds, 34 corporate investors (including corporate venture capital funds), and 17 angel groups or investors. Thirteen investors made five or more investments in the spin-outs attributed to MRC funded research, as set out in the table below.

The table highlights the important role of institutions with locally or sector specific objectives (including those attached to or working in partnership with universities) in capitalising spin-outs. For example, Oxford Sciences Innovation, Cambridge Enterprise, and UCL Business all have objectives to capitalise spin-outs emerging from the research undertaken within the university. Local variations in the availability of this infrastructure is likely to contribute to the spatial patterns in equity investment observed above.

Investor	Description	No. of investments in spin-outs attributed to MRC research
Oxford Sciences Innovation	Oxford Sciences Innovation seeks to invest in companies operating in the medical, computer science, industrial consumer technology, data analytics and engineering sectors. It was founded in partnership with the University of Oxford.	15
Cambridge Enterprise	Cambridge Enterprise operates as a subsidiary of the University of Cambridge. The firm invests the University's seed to commercialize ideas and share knowledge gained from research within the University.	14
Scottish Enterprise	Scottish Investment Bank is Scottish Enterprise's investment arm investing to invest in small to medium businesses that are based in Scotland.	14
Parkwalk Advisors	Parkwalk Advisors is a venture capital fund based in London, United Kingdom. The firm makes venture capital investment in technology companies that have spun out from UK universities and similar institutions.	12
Oxford Spin-out Equity Management	Oxford Spin-out Equity Management manages Oxford University's shareholdings in its spin-out companies and seeks ways of maximizing the value of its equity stakes.	11
Syncona	Syncona is a venture capital investment subsidiary of Wellcome Trust that is focused on investing in the healthcare and life science sectors.	10
TRI Cap	TRI Cap is one of Scotland's business angel group founded in the year 2004.	9
Archangel Investors	Archangel Informal Investments is an angel investment firm based in Edinburgh.	9
SV Health Investors	SV Health Investors is a venture capital firm based in Boston, Massachusetts. The firm prefers to invest in the medical device, life sciences, healthcare services and digital health and biotechnology sectors.	7
UCL Business	UCL Business is a technology development and commercialization transactions firm that invest through its UCL Technology Fund.	7
Albion Capital	Albion Capital invests in high growth ventures, social infrastructure and quoted equities across the different funds. The firm supports outstanding entrepreneurs who have demonstrated product-market fit and wish to optimize and scale their business rapidly.	5
Barwell	Barwell is a Glasgow, United Kingdom based venture capital firm which focuses on investing companies within the life sciences, software, oil and gas sectors	5
SR One	SR One is the corporate venture capital investment arm of Glaxosmithkline. It is based in Massachusetts with additional offices in Conshohocen, Pennsylvania; London, England and San Francisco,.	5

One third (by number of investments made) of investors in spin-outs attributed to MRC research were located overseas. As illustrated in the figure below, there was a dependency on investors based in North America. There was little evidence of significant capital flows from Europe or Asia into spin-outs attributed to MRC funded research.

⁸ Where investments were made on a syndicated basis, each investor associated with the funding round is counted separately in this total – implying that was an average of three investors associated with each investment.



Figure 1.7: Geographical distribution of investors in spin-outs attributable to MRC research

Source: Pitchbook, UK headquartered firms only

1.3 Exits

1.3.1 Exits achieved by spin-outs attributed to MRC funded research

A total of nine spin-outs attributed to MRC funded research (i.e. seven percent of the total number established) reached an exit for their investors through an IPO or through a corporate acquisition:

- IPOs: As noted above, four companies completed an IPO by the end of 2018 Nightstar, Orchard Therapeutics and MeiraGTx, and Bicycle Therapeutics. These companies share common characteristics:
 - Except for Bicycle Therapeutics, they are focused on the development of gene therapies and have developed a portfolio of candidates extending beyond those associated with the grants awarded by MRC.
 - The three companies now have a global reach with a presence in the US and are listed on the NASDAQ. It is possible to speculate that this reflects desire to access the greater depth of capital markets, although where the PIs concerned were interviewed, they were not close to the current commercial strategy and these issues were not discussed during interviews.
 - Leading candidates are largely in or have concluded Phase II trials at present. Orchard Therapeutics reports it will seek FDA approval for its gene therapy for ADA in 2019, which emerged directly from MRC funded research.
 - The companies have attracted interest of large pharmaceutical firms. Nightstar Therapeutics announced a definitive agreement to be acquired by Biogen for £688m⁹ in 2019 (as highlighted below). MeiraGTx has recently announced talks with Johnson & Johnson with respect to a possible partnership agreement that would lead to an additional £100m in working capital.
- **Corporate acquisitions:** Six spin-outs (5 percent of the total established) generated an exit for their investors through a corporate acquisition by 2018. Details of these acquisitions are set out in the table below.

⁹ Note that this transaction was in dollar terms and the sterling value was correct as of 30th August 2019.

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Company	Relevant MRC funded research	Acquired by	Deal Size
iOX Therapeutics – developer of cancer immunotherapies established in 2015.	Attributed to two MRC grants: programme funding for the MRC Immunology Unit and an award specifically to investigate vaccination strategies enhance tumour specific T cell responses.	SalvaRx - UK based immunotherapy developer, itself acquired in January 2019 by Portage Biotech (Canada) for £71.7m.	Undisclosed.
Activiomics – developer of label- free mass spectrometry technologies for biomarker development.	Attributed to collaborative project (with AstraZeneca) to explore the role of PI 3-kinases in haematological cancers.	hVIVO (formerly Retroscreen) – UK headquartered CRO providing human disease models to accelerate drug discovery in infectious and respiratory diseases.	£3.1m
Immago Biosystems – developer of antibody based cancer therapies.	Attributed to 2012 Confidence in Concept Award to Oxford University.	Hansa Biopharma – pharmaceutical company headquartered in Sweden.	Undisclosed
Proaxsis – developer of technologies to capture and measure protease biomarkers.	Attributed to 2012 Confidence in Concept Award to Queen's University Belfast.	NetScientific UK – UK headquartered healthcare group focused on developing early and mid-stage technology companies in diagnostics, digital health and therapeutics.	£1.2m
Imanova – developer of PET and MRI techniques to raise productivity in early drug development	Attributed to 2010 award to King's College London to develop quantitative PET imaging probes for neuroinflammation.	Invicro – UK based CRO providing data analysis and software for pre-clinical imaging	Undisclosed
Nightstar Therapeutics – developer of gene therapies for ocular diseases.	Attributed to 2013 award to develop gene therapy to treat Stargardt Disease. There is uncertainty as to whether this case should be treated as a licensing agreement or a spin-out, as the account given by the PI suggested that the spin-out was initially founded to commercialise other therapies.	Biogen – large US biotechnology firm, specialising in neurological and autoimmune diseases.	£688.1m

1.3.2 Exits in context of the overall sector

By early 2019, 54 firms founded since 2008 that were active in the pharmaceutical and biotechnology, healthcare technology systems, healthcare devices, and digital health sectors completed an exit for their investors through an IPO or a corporate acquisition. Again, assuming the OLS Biopharma and Medical Technology database gives a sufficiently accurate measure of the number of start-ups in the sector over the period, this equates to 3 percent. This indicates that spin-outs attributed to MRC research were more likely to deliver an exit for their investors than average. In terms of attained values:

- IPOs: There were 11 IPOs over the period, through which the firms concerned raised a total of £643.6m. Spinouts attributed to MRC funded research accounted for 50 percent of this total. Other companies to raise significant funding from capital markets included Adaptimmune (£127.6m) and Autolus (£112.6m), both of which originated in research funded by the MRC and other Research Councils.
- Acquisitions: There were a further 100 completed acquisitions deals with a total value of £4.2bn (including contingent pay-outs) to which the main contribution of spin-outs attributed to MRC funded research was the sale of Nightstar Therapeutics described above. Other deals included six major transactions involving five therapy developers and one developer of biosensors. These companies included Ziarco (to Novartis for £815.9m), Ziylo (to Novo Nordisk for £617.1m), Tusk Therapeutics (to Hoffmann-La Roche for £585.1m), Convergence

Pharmaceuticals (to Biogen for £429.1m), F-Star Gamma (to Denali Therapeutics for £349.9m) and iOmet (to Merck for £270.1m). Each acquirer was headquartered overseas, highlighting the acknowledged shortage in domestic corporate exit opportunities and the risk that the long-term economic impacts associated with the exploitation of the underlying intellectual property are realised overseas.

1.4 Firm values

Valuations of firms provide a measure of the net economic value that has accumulated in the spin-outs attributed to MRC funded research. In perfect markets with no transaction costs, the price investors are willing to pay will reflect risk weighted expectations of future profits over and above the risk-free rate of return (and in turn, those profits should reflect the value of future health impacts associated with the adoption of the technologies being developed)¹⁰.

Records from Pitchbook capture the valuations of firms at the point they receive investment (where disclosed). Analysis of the most recent valuation of companies (including current enterprise values for those firms that were listed on public markets) suggests that the total value of spin-outs attributed to MRC funded research totalled £2.9bn by August 2019.

1.5 Attribution to MRC funding

There are questions as to how far these results can be attributed directly to the MRC grants awarded, as PIs may have – in principle - secured funding from other private, public or charitable sources in the absence of the MRC (producing similar outcomes). This section provides summary results of more detailed statistical analysis focused on comparing marginal applicants to the Development Pathway Funding Scheme (DPFS)¹¹, part of the MRC directed translational research portfolio, to explore questions of what may have occurred in the absence of this programme.

1.5.1 Key hypotheses

It is anticipated that grants awarded by the MRC could have two distinct types of effect on spin-out activity:

- Likelihood spin-outs are established: In principle, MRC funding for preclinical and/or clinical research may allow research teams to progress the translation of their underlying technologies, increasing the likelihood that they reach a point at which the costs of establishing a spin-out are justified by its potential commercial success. There is also a possibility that research teams that are not awarded funding go on to establish a spin-out to attract private resources to fund the on-going development of the technology (for example, if they are unable to attract academic or charitable funding from other sources). There is a degree of ambiguity over expected impact of the programme on the likelihood of a spin-out.
- Performance of the spin-out: However, MRC funding would also lead to de-risking of the underlying technology by enabling PIs to develop a more complete data package regarding its likely efficacy. This could ease the difficulties faced by the spin-outs in attracting external investment to fund their ongoing activities, producing longer term effects on the speed with which it can progress the underlying technologies. There was also evidence from interviews with opinion leaders that receipt of MRC funding acts a quality signal to investors. As such, the prior expectation is that MRC funding would enable founders to access capital markets more readily, attracting greater levels of investment.

¹⁰ While there will be issues in that spin-outs may grow at the expense of competitors or crowd out other activities. However, it might be assumed that the activities displaced or crowded earn a 'normal' rate of return and as such these issues can be put to one side.

¹¹ This analysis focuses on the DPFS as the data on declined applicants needed was not available for other initiatives.

1.5.2 Database of spin-outs

This analysis drew on MRC records of PIs and Co-Is that were awarded grants through the DPFS and those that applied but were declined funding. To complete the following analysis, it was necessary to construct a database of spin-outs established by those awarded funding and those that applied but were not successful.

This database was constructed by searching the Companies House register for companies established since 2008 where the Principal Investigator was named as a founding Director. This process over-identified the number of companies that could be plausibly connected to the research programme associated with the funding applications made. Several PIs were named as Directors of companies that had no direct connection to the development of new technologies (i.e. they could not be characterised as 'spin-outs'). This included instances where the PI was named as a Director of scientific societies, clinical practices, or property management companies. These companies were excluded from the database.

Comparisons were also made between the abstract associated with the grant application and the pipeline described on the website and other public documentation associated with the firm. For those awarded grants, information was also drawn from Researchfish and interviews with PIs (where available) to provide further confirmation. If a link could not be established (e.g. if the company had no website), then these companies were excluded from the database. This process identified 15 spin-outs associated with those awarded DPFS grants and five associated with applications that were declined.

There is a high level of consistency between the administrative data, Researchfish and the PI interviews. The only inconsistency identified arose from companies established recently (i.e. since mid-2018) which do not appear in Researchfish, likely due to the lagged nature of the data. There were also several companies established by PIs recently without websites, which may be spin-outs but could not be definitively connected to the research (and these have not been included in the analysis).

1.5.3 Analytical approach

The aim of this analysis is to isolate the incremental effect of the grants awarded through the DPFS on both the likelihood that an academic research team establishes a commercial vehicle to exploit the research and the underlying performance or growth of those spin-outs. Disentangling the causal effect of the grants awarded is challenging as the intellectual property underpinning the spin-out is often developed over a sequence of grants (and in many cases, relevant fundamental science will also have been supported by the MRC). The relationship between MRC funded research and the pipelines of the relevant firms is also complex. In some cases, MRC funding clearly contributed to the development of the technology platform upon which the firm's pipeline was based. In others, MRC funding only supported the development of a single candidate (raising questions as to how far the funding was a causal factor in the outcomes described above).

These issues can be explored with more precision by drawing an appropriate comparison group of research teams that did not receive funding through the programme but were otherwise equivalent to those that did. PIs making applications for funding through the programme but were declined are likely to share many characteristics with those did receive grants. However, as applications are judged both on their scientific and commercial merits, these differences may merely be a product of the quality of the underlying research programme rather than an effect of the grant awarded.

This problem can be addressed by exploiting the process through which grants are awarded. The architecture of the resource allocation process creates a formal discontinuity between those awarded grants and those that were not, at the minimum scoring threshold for each round. It can be assumed that while those awarded grants and those who were not will differ systematically on an overall basis, randomness in the scores in the immediate vicinity of this minimum scoring threshold will mean that the observed and unobserved characteristics of the two groups will be also random. As such, comparisons between those just exceeding the minimum scoring threshold and those that just fell

short should provide robust measures of the causal effects involved, as the design has an interpretation close to that of a Randomised Control Trial. However, these findings are considerably less generalizable, as they only capture the effect of the programme on the marginal applicant (i.e. those that 'just made it').

1.5.4 Comparisons between marginal applicants

The findings of this analysis are illustrated in the following figure:

- At the margin, the DPFS did not have a statistically significant effect on increase the likelihood a team establishes a spin out.
- However, DPFS appears to have had a significant (incremental) causal role in enabling spin-outs to realise the underlying commercial value of the research that was funded and its ability to secure equity investment. At the margin, those PIs receiving an award from DPFS raised an average of £4.0m in equity investment relative to just £40,000 amongst those declined funding. The average valuation of firms established by PIs awarded funding was £9.4m relative to £90,000 amongst those declined funding.
- Given that the DPFS is central driver of the commercialisation outcomes described in the preceding passages, it suggests that a high share of the overall economic outcomes associated with the MRC's investments in translational research would not have occurred in its absence.
- The implication of these findings is that in the absence of the DPFS, PIs may establish spin-outs before they are ready (for example, if the data package is insufficiently complete), and struggle to realise the potential value of their intellectual property assets. As the PI interviews were focused on those that received grants, it has not been possible to explore the challenges in more depth.



Figure 1.8: Comparisons between marginal applicants to DPFS

Source: MRC monitoring records, Companies House, Ipsos MORI analysis