UK biotech financing and deals in 2015/16

Money, momentum and maturity
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#BIAfinance
Foreword

The biotech sector has enjoyed a remarkable surge over the past couple of years, evident across the globe. The latest data, compiled by the BIA in partnership with Evaluate and the London Stock Exchange, indicates continued momentum for the UK industry in 2015.

Whilst IPO activity may have cooled off, last year saw an unprecedented rise in follow-on funds raised on the London Stock Exchange. This was particularly evident on AIM, with almost four times the amount raised than the previous year, accounting for over 60% of the total amount raised by biotech companies on the LSE (versus 23% in 2014).

Another standout story for 2015 was the level of VC activity in the sector, with £489m raised in the UK – that’s up a staggering £166m from 2014 – helped by Immunocore’s record-breaking £205m round. The UK continues to extend its lead in Europe, accounting for over a third of total European VC funding.

A marked trend is towards larger financing rounds of fewer but perhaps better positioned businesses, as investors move away from the historical ‘drip-feed’ approach. This will enable quality UK management teams to focus on delivering value with an increased level of maturity.

Although the UK and Europe as a whole still lag behind the US and its leading clusters, these are all promising trends as we look to develop the UK as the third global biotech cluster, building on its established lead in Europe.

There are also some advantageous differentiations developing in the UK versus the US. Firstly, London has established itself as a hub for IP commercialisation businesses in recent years, providing the longer-term patient investment and support required by companies to succeed. Secondly, we’re starting to see the nascent crowdfunding sector have an increasing impact on biotech here in the UK, ahead of the US, with AIM-listed Scancell the first company to apply crowdfunding to the public markets. This is a trend to keep a closer eye on in 2016.

At the time of writing we await the result of the EU Referendum in the UK. With other global political events in play for 2016 - such as the US Presidential election - the crystal ball remains fogger than usual in terms of predicting the macro-economic and political environment, both at a national and international level, which undoubtedly has a significant impact on sector financing.

That said, the first half of 2016 has seen private fundraising continuing to grab headlines, with the UK’s MISSION Therapeutics recording a £60m Series C in February led by Imperial Innovations and Woodford Patient Capital Trust. The IPO window also remains ajar even in these chillier months with Shield Therapeutics, and most recently Mereo BioPharma, successfully listing on AIM.

However what is clear is that despite signs of continued momentum and maturity in the funding of the sector, from the data for 2015 and our experience so far in 2016, there is no room for complacency. For example, the lack of reported seed capital for UK companies in 2015 raises a potential red flag and underlines the importance of effective support for early-stage companies through fit for purpose innovation policy from the government.

Given the strong R&D pipeline coming through the UK and the impressive rate of regulatory approvals, the sector is in good shape and there is great potential to build on. Ensuring that early-stage companies have access to kick-start innovation funding, such as that offered through the Biomedical Catalyst, is essential to take start-ups to a stage from where they can effectively leverage private capital.

A shared focus from government, industry and investors on how we can sustain start-up momentum, alongside scaling-up UK life science companies into the cohort of mid-tier companies the country needs to feature as a top three global cluster, is what is required in 2016 to build on current momentum – whatever the rest of the year holds.
Key Findings

Overview of key findings

- **UK companies accounted for over a quarter** (£178m, 27%) of the amount raised by European biotechnology company IPOs in 2015.

- In 2015, **AIM-listed biotechs raised a huge £574m in further capital** – over 60% of the total money raised by biotechnology companies on the London Stock Exchange.

- **UK venture capital activity also hit a high in 2015, with £489m raised versus £323m in 2014.** The gap between UK venture funding and the rest of Europe continues to widen, with the UK contributing over a third of the European total in 2015.

- **Average VC round sizes again increased in 2015,** with a trend for fewer but larger rounds.

- In 2015, **M&A was not just dominated by the industry’s big players,** with relatively newly-listed companies such as Circassia and Clinigen recording £100m plus deals.

- **The UK remains an R&D powerhouse, with the 585 pipeline projects in development,** far outstripping other European countries. This includes the highest number of phase 3 projects in Europe.

- **The rate of both US and European approvals for UK companies is well ahead of European peers.** Despite its smaller number of biotech companies, the UK reported more regulatory wins than Massachusetts.

BIA analysis

- 2015 data and experience to date in 2016 indicate **continued momentum for the UK biotech sector with encouraging trends in follow-on funding, VC activity, the strength of the R&D pipeline and rate of regulatory approvals** which are promising as we look to develop the UK as the third global cluster.

- However, in light of uncertain macroeconomic and global political dynamics as we head into the second half of 2016 **there is no room for complacency.**

- The lack of reported seed capital in 2015 is a potential red flag and **underlines the importance of effective support for early-stage companies** through fit for purpose government innovation policy.

- A **shared focus from government, industry and investors on how to sustain the UK’s start-up momentum, alongside scaling-up UK life sciences companies,** is what is required in 2016 to build on current momentum – whatever the rest of the year holds.
Public market activity

UK biotechnology company IPOs

From 2014’s IPO high point of eight UK companies listing across a range of indices, 2015 was a much quieter affair, producing only five UK stock market debuts. The £176m raised in 2015 was also down significantly from the £476.2m banked in 2014.

In the absence of big ticket IPOs like Circassia, Horizon Discovery and Midatech, 2015’s biggest listing was Adaptimmune, which chose to float not at home, but in the US, tapping into the huge interest in T-cell therapy. The £127.8m contribution from Adaptimmune accounted for more than 70% of the total amount raised by UK companies in 2015.

Although listings were down in the UK many other European companies failed to record any IPOs in 2015. Only France managed to beat the UK total with seven IPOs raising £179.4m, helped by many of the companies spinning out of larger businesses.

The view in 2016

The global biotech industry has seen a widely acknowledged slowdown in IPOs in the first quarter of 2016, influenced in part by wider macro-economic factors and factors such as the US presidential election. With these factors still in play, it seems unlikely that 2016 will be a bumper year for biotech company IPOs.

Despite this, the window remains ajar and we continue to see UK companies commit to going public, such as Shield Therapeutics who successfully listed on AIM in February.

UK biotechnology company IPOs

Source: EvaluatePharma®
### Top UK biotechnology company IPOs, 2015

<table>
<thead>
<tr>
<th>Company</th>
<th>Ticker</th>
<th>Exchange</th>
<th>Amount Raised (£m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adaptimmune</td>
<td>ADAP</td>
<td>Nasdaq</td>
<td>127.8</td>
</tr>
<tr>
<td>Diurnal</td>
<td>DNL</td>
<td>LSE AIM</td>
<td>25.3</td>
</tr>
<tr>
<td>Redx Pharma</td>
<td>REDX</td>
<td>LSE AIM</td>
<td>15.0</td>
</tr>
<tr>
<td>Evgen</td>
<td>EVG</td>
<td>LSE AIM</td>
<td>7.0</td>
</tr>
<tr>
<td>Motif Bio</td>
<td>MTFB</td>
<td>LSE AIM</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®

### Biotechnology company IPOs, Europe and the US, 2015

<table>
<thead>
<tr>
<th>Region</th>
<th>Total (£m)</th>
<th>Average (£m)</th>
<th>Largest (£m)</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>179.4</td>
<td>25.6</td>
<td>61.2</td>
<td>7</td>
</tr>
<tr>
<td>UK</td>
<td>178.0</td>
<td>35.6</td>
<td>127.8</td>
<td>5</td>
</tr>
<tr>
<td>Belgium</td>
<td>86.7</td>
<td>43.4</td>
<td>62.1</td>
<td>2</td>
</tr>
<tr>
<td>Europe*</td>
<td>620.5</td>
<td>32.7</td>
<td>127.8</td>
<td>19</td>
</tr>
<tr>
<td>US*</td>
<td>2243.2</td>
<td>28.8</td>
<td>136.1</td>
<td>78</td>
</tr>
</tbody>
</table>

*average annual exchange rates used
Source: EvaluatePharma®

### Number of European biotechnology company IPOs, 2015

- France: 5
- UK: 2
- Belgium: 5
- Other: 7

Source: EvaluatePharma®

### Amount raised by European biotechnology company IPOs, 2015

- France: 27%
- UK: 27%
- Belgium: 13%
- Other: 32%

Source: EvaluatePharma®
**Dr Neil Murray, CEO, Redx Pharma**

The past year has been transformational for Redx: we expanded our operations and achieved a number of scientific milestones. One of the catalysts for this progress was our successful flotation on the London Stock Exchange’s AIM market in March 2015. At IPO, we raised £15m (gross), which helped us to grow our world-class capability in small-molecule drug discovery and development in immuno-oncology, cancer stem cells, antimicrobial resistance and autoimmune diseases.

The IPO offered an opportunity for us to invest heavily in our programs. Since flotation, we have seen the benefit of this investment with excellent progress across our pipeline and we anticipate moving into clinic with our lead programs targeting cancer and antimicrobial resistance early in 2017.

Joining AIM has been beneficial for Redx in terms of the initial capital injection, but also in providing us with access to the public markets for further funding to support our ambitious growth plans.

The exposure we have gained from being a quoted company has enhanced our reputation in our chosen fields, opening up additional opportunities and helping us establish further industry connections.

“Joining AIM has been beneficial for Redx in terms of the initial capital injection, but also in providing us with access to the public markets for further funding to support our ambitious growth plans.”

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**Carl Sterritt, Founder and CEO, Shield Therapeutics**

Shield Therapeutics is a UK-based specialty pharmaceutical company focused on the commercialisation and development of secondary care-focused pharmaceuticals. The Company’s lead product - Feraccru - received marketing authorisation across the European Union in February 2016, which Shield successfully combined with an IPO on the AIM market of the London Stock Exchange, raising £32.5m of growth capital from new and existing investors.

The funds raised at IPO are now being used to commercialise Feraccru (which is estimated to have an achievable global peak annual sales opportunity in excess of £500m) via a phased roll-out across Europe in 2016 and 2017, and to fund the additional clinical trials required to expand the product’s geographic and indication reach.

Feraccru is a novel and effective oral ferric iron-based prescription pharmaceutical that is licensed to treat iron deficiency anaemia in patients with inflammatory bowel disease and is primarily targeted at patients who have failed treatment on oral ferrous products, or for whom such treatment is unsuitable.

Shield’s successful IPO was a transformational event in the life of this ambitious growth company. Our in-house commercialisation strategy seeks to retain greater value for shareholders, whilst providing patients with an innovative product, and the IPO provided us with the new capital to deliver our commercialisation plans. We are now well on the road to becoming a fast-growing, independent, international specialty pharmaceutical company and, due to the strength of our product and team, I look forward to the future with great excitement.

“Shield’s successful IPO was a transformational event in the life of this ambitious growth company.”
The London Markets and follow on activity

James Clark, Business Development Manager, Primary Markets, London Stock Exchange

2015 was an impressive year for biotech companies raising capital on the London Stock Exchange, with just over £900m raised across IPOs and further issues. There were two significant transactions on the Main Market in the biotech space in 2015. The first is evidence of London’s growing reputation amongst US biotech firms, with PureTech raising £108m on the Main Market (despite being excluded from the graph below, based on FTSE sub-sector Biotechnology). The second significant transaction on the Main Market was by Circassia who, having completed a highly successful IPO in 2014, returned to the market to raise £275m to support the acquisitions of Aerocrine AB and Prosonix Limited. The 100% primary deal priced at a premium of 0.37% showing large demand for the story and London’s ability to absorb large secondary issues.

AIM also had a successful year with AIM listed biotech firms cumulatively raising almost £600m in further capital. Highlights include Benchmark Holdings returning to the market to raise £186m to finance the acquisition of INVE Aquaculture Holding B.V and Clinigen raising £135m to support the acquisition of Idis Group Holdings Ltd. AIM also saw five biotech IPOs, the highlights including Motif Bio which is now 95% above offer price having opened up 75% on debut. Faron Pharmaceuticals Oy, a Finnish clinical stage drug discovery and development company focusing on acute organ traumas, raised £10m to fund the initial pan-European Phase III INTEREST trial in respect of Traumakine and to provide working capital.

Combining AIM and Main Market data what we can observe is a large display of confidence in the long term value of the UK public markets as a source of growth capital for returning issuers in the biotech industry. Reminding us that the real value of a public listing is not just the fundraising at IPO, but the ability to continue to tap public markets as a company’s strategic objectives expand.

“the real value of a public listing is not just the fundraising at IPO, but the ability to continue to tap public markets as a company’s strategic objectives expand”

Biotechnology money raised on the London Stock Exchange

Source: London Stock Exchange. Data based on FTSE Biotechnology sub-sector, therefore excludes PureTech’s IPO on the Main Market
Steve Harris, CEO, Circassia

The last year has been an important period of transformation for Circassia. In June 2015, the company successfully raised £275m to fund two strategic acquisitions. These were highly complementary to Circassia’s existing allergy franchise, with its lead programme’s pivotal phase III study progressing on track to report the following year in Q2 2016, and broadened the company’s commercial capabilities and pipeline. The acquisitions brought marketed speciality products and established commercial infrastructure in the US and Europe’s largest market, Germany, while also extending the company’s portfolio into the field of respiratory medicine.

Subsequent progress across the enlarged business has validated the acquisition strategy. In the six months following the deals, sales of the newly-acquired NIOX® asthma management products increased dramatically, growing 32% on the same period the year before, and the lead respiratory product received approval from the MHRA. During the same period, Circassia invested significantly to expand the company’s commercial presence, with major growth in its US sales force and marketing and market access teams, as well as beginning the process of establishing a broader direct presence in Europe. Not only is Circassia now well positioned to promote its own specialty products, its commercial infrastructure is a strategic asset providing an attractive platform for further acquisition and in-licensing.

This rapid progress was only possible because of the support of investors in the UK market. With a robust investment case, the company was able to attract the significant funding required to accelerate its transformation into a commercial-stage business with the finances to drive its future growth. Circassia has now joined the growing cohort of UK-listed life science companies making the transition into genuine product businesses, which are in turn a reflection of the increasing strength of the UK industry.

“Circassia has now joined the growing cohort of UK-listed life science companies making the transition into genuine product businesses, which are in turn a reflection of the increasing strength of the UK industry.”

Michael Hunt, CFO, ReNeuron

ReNeuron was fortunate to be among a cohort of AIM-quoted life science businesses to have secured significant follow-on funding during 2015 – a year marked by a substantial increase in the amount of follow-on funding received in the sector, both on AIM and on the main market.

Despite the improved fundraising outcome last year, we still see the availability of biotech funding on the UK public markets as concentrated in the hands of too few institutional investors, be they generalist or specialists in life science investing. This can create a significant degree of uncertainty of outcome in terms of quantum raised, especially if the investee business is looking to attract any of these notable investors into their stock for the first time.

Our own 2015 follow-on funding amounted to £68m, providing ReNeuron with cash resources to take its lead cell-based therapeutic programmes targeting vascular and ophthalmic diseases into late-stage clinical development over the next two years. The funding has also allowed us to invest further into new programmes, such as our exosome nanomedicine platform targeting cancer.

“The funding has also allowed us to invest further into new programmes”
Venture capital activity

Overall trends

While the number of UK IPOs may have declined, investors’ appetite for venture finance was stronger than ever in 2015 as they continued to see lucrative exits. The massive £205m raised by Immunocore helped the UK hit a high for private investment, accounting for over 40% of the UK total and set a record as the second largest European private round to date.

Once again the pronounced financing trend in the UK was for fewer, but larger rounds, demonstrating investors’ desire to shepherd sure bets towards exit with as little dilution as possible.

The gap between UK and venture funding and the rest of Europe continued to widen. Only the Netherlands come anywhere near the UK total, with £304.1m raised in the year. So strong was the UK that it made up more than a third of total European financing.

Unsurprisingly, the US states of California and Massachusetts beat European fundraising hands down, netting £1.84bn and £1.67bn respectively, reflecting the large biotech clusters in the region and investor numbers and experience. However, the total for Massachusetts did include the history-making $450m investment in Moderna, while California was boosted by two $200m plus rounds for Denali Therapeutics and Stem CentRx.

The view in 2016

The trend towards larger rounds seems to have continued into 2016, as illustrated by MISSION Therapeutics’ £60m Series C – reported to be the largest European round in the first quarter of the year. The amount would have placed in the top three UK venture funding rounds in 2015.

UK venture capital investment, 2010 to 2015

Source: EvaluatePharma®
Top UK venture financing rounds, 2015

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Financing Date</th>
<th>Financing Round</th>
<th>Investment (£m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Immunocore</td>
<td>Jul-15</td>
<td>Series Undisclosed</td>
<td>205.0</td>
</tr>
<tr>
<td>2</td>
<td>Mereo BioPharma</td>
<td>Jul-15</td>
<td>Series A</td>
<td>76.5</td>
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<tr>
<td>3</td>
<td>Kymab</td>
<td>May-15</td>
<td>Series B</td>
<td>32.8</td>
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<tr>
<td>4</td>
<td>Autolus Therapeutics</td>
<td>Jan-15</td>
<td>Series A</td>
<td>30.0</td>
</tr>
<tr>
<td>5</td>
<td>PsiOxus Therapeutics</td>
<td>May-15</td>
<td>Series C</td>
<td>25.0</td>
</tr>
<tr>
<td>6</td>
<td>Freeline Therapeutics</td>
<td>Dec-15</td>
<td>Series A</td>
<td>25.0</td>
</tr>
<tr>
<td>7</td>
<td>NightstaRx</td>
<td>Nov-15</td>
<td>Series B</td>
<td>23.1</td>
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<tr>
<td>8</td>
<td>KalVista Pharmaceuticals</td>
<td>Jul-15</td>
<td>Series B</td>
<td>21.1</td>
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<tr>
<td>9</td>
<td>Kesios Therapeutics</td>
<td>Dec-15</td>
<td>Series A</td>
<td>19.0</td>
</tr>
<tr>
<td>10</td>
<td>reViral</td>
<td>Sep-15</td>
<td>Series A</td>
<td>13.7</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®

Venture capital raised, Europe and the US, 2015

<table>
<thead>
<tr>
<th>Region</th>
<th>Total Investment (£m)</th>
<th>Average (£m)</th>
<th>Largest (£m)</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
<td>UK</td>
<td>488.7</td>
<td>32.6</td>
<td>205.0</td>
<td>15</td>
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<tr>
<td>Europe</td>
<td>1386.0</td>
<td>24.3</td>
<td>252.0</td>
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<tr>
<td>Massachusetts</td>
<td>1669.9</td>
<td>26.1</td>
<td>295.4</td>
<td>64</td>
</tr>
<tr>
<td>California</td>
<td>1843.1</td>
<td>18.6</td>
<td>162.9</td>
<td>99</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®

Tim Haines, Managing Partner, Abingworth

The UK life sciences sector continues to be an excellent place for investment. We have world class science, experienced management and innovative entrepreneurs creating a vibrant environment for building successful companies.

We believe the sector has come of age as demonstrated by drugs significantly extending lives, for example PD-1 inhibitors changing the landscape of cancer immunotherapy, and breakthrough medicines curing diseases such as hepatitis C. Novel technologies continue to offer tantalising promise, including CRISPR gene editing, which has the potential to translate into clinically meaningful benefit in a wide range of disease areas.

As supported by the 2015 data the sector, particularly the UK, continues to attract significant investment, with increasing interest from our US co-investors keen to participate in earlier rounds. They view European biotech as a fertile hunting ground where the science is outstanding and valuations are often lower than their US competitors.

As for our own recent UK activity, we are excited about the potential for the early-stage company, Kesios Therapeutics. In 2015 we invested in the Series A round for this oncology spin-out from Imperial College London led by Paolo Paoletti, formerly President of Oncology at GSK, which is about to start clinical trials for multiple myeloma.

As always the outcome of investing in life science is unpredictable, but we are very optimistic that we are on the cusp of the most exciting and innovative era in biotechnology, which will translate into positive outcomes for entrepreneurs, investors and, most importantly, patients.

“We are very optimistic that we are on the cusp of the most exciting and innovative era in biotechnology”
Anker Lundemose, CEO, MISSION Therapeutics

MISSION Therapeutics announced it had raised £60m through a Series C financing in February 2016. This took the total amount raised to date by the Company up to nearly £90m.

As a global leader in drug discovery for selective targeting of deubiquitylating enzymes (DUBs) to treat cancer, neurodegenerative and other diseases the Company attracted one of the highest profile investor syndicates in Europe. The syndicate was jointly led by Imperial Innovations and new investor Woodford Patient Capital Trust Plc with follow-on investment from existing shareholders Sofinnova, SR One, Roche Venture Fund and Pfizer Venture Investments.

“the Company attracted one of the highest profile investor syndicates in Europe”

Despite significant efforts within the pharma industry there is a lack of DUB inhibitors in clinical development and MISSION, backed by industry as well as financial investors, is focused on using its world-class, DUB discovery chemistry platform to discover and develop novel small molecule drugs in an area seen to be potentially as diverse and exciting as the Protein Kinases. DUBs are involved in multiple cellular processes including DNA damage and cell proliferation. Inhibition of these enzymes appears to have the potential for significant leaps forward in therapeutic effect in areas such as cancer and Parkinson’s disease.

The Series C provides a runway to deliver phase 1 results and 2016 will see MISSION progressing our advanced programs, including our USP30 inhibitor for Parkinson’s, into regulatory preclinical development and deepening our pipeline.

A bumper year for Series A rounds

In what must be encouraging news for smaller companies, the second biggest chunk of total UK venture funding went to Series A rounds. In total, five of the UK top 10 were Series A rounds and a further three were Series B. Mereo BioPharma led the Series A investment with its £77m raise, which was also globally the ninth biggest fundraising in 2015. Less positive was the apparent lack of reported seed capital in the UK companies included in this analysis. In 2014, £29.4m went to seed stage companies, where deal terms were announced.

Average round sizes again increased in 2015, as investors continued to fund a smaller number of companies with larger money pools, demonstrating the increasing role “patient capital”, or long-term investment, is playing in the UK sector.

In 2015 the average UK round was £32.6m, more than double the 2014 average of £15.4m. This change in funding pattern was linked to the number of UK financing rounds falling from 24 in 2013, to 21 in 2014 and 15 in 2015 – the lowest count in the last six years.
### UK venture capital raised, by round, 2010 to 2015

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2014</th>
<th>2013</th>
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<tr>
<td></td>
<td>Total Investment (£m)</td>
<td>Count</td>
<td>Total Investment (£m)</td>
</tr>
<tr>
<td>Seed Capital</td>
<td>-</td>
<td>-</td>
<td>29.4</td>
</tr>
<tr>
<td>Series A</td>
<td>172.2</td>
<td>6</td>
<td>116.0</td>
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<tr>
<td>Series B</td>
<td>77.6</td>
<td>4</td>
<td>152.8</td>
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<tr>
<td>Series C</td>
<td>26.3</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Series D</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Series E</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Series Undisclosed</td>
<td>212.6*</td>
<td>3</td>
<td>24.7</td>
</tr>
</tbody>
</table>

### UK venture capital investment, early stage rounds, 2010 to 2015

- Includes Immunocore’s £205m investment.
- Source: EvaluatePharma®
Supporting innovation

The lack of reported seed capital for UK companies in 2015 raises a potential red flag. Although this data point is problematic in the sense that one cannot be sure of unreported funding, the 2015 figures are well down on the £29.4m 2014 figure. This underlines the importance of effective support for early-stage companies through fit for purpose innovation policy from the government, in the form of both incentives and funding.

A great deal of current policy is welcome, effective and is of fundamental importance to the life sciences sector. For example, R&D tax credits, the EIS and SEIS schemes and the Patent Box. However, the UK government needs to keep these incentives under review to ensure they are optimal and globally competitive in order to support the UK life sciences sector.

One incentive worthy of review is the entrepreneurs’ relief, which currently does not work for life sciences businesses as repeated capital raises mean that in the vast majority of cases the founders will never hold the 5% share threshold required to be eligible for the relief. This results in a perverse incentive against scale and growth and creates a barrier for entrepreneurs to “come around again” in the sector, having lost out on a theoretically available incentive despite building a personal company at risk over several years.

Following the 2015 Comprehensive Spending Review, the government also needs to ensure that innovation policy and funding remains fit for purpose and globally competitive. To do this the successful Biomedical Catalyst scheme needs to be recommitted to and refunded in order to get companies off the ground and to a stage where they can leverage in private capital. The government also needs to ensure that new finance products in support of innovation, including loans, work within the context of the life sciences funding landscape.

Jonny Ohlson, Founder, Director and CEO, Touchlight Genetics

However hard biotech entrepreneurs try to position it, the reality of investment in biotech is that it is in the main high-risk and long-term. This profile has been the cause of a paucity of funds looking at early-stage investments, which when combined with the two other industry truisms - it will take longer and cost more - make the funding options open to the biotech entrepreneur few and far between.

Yet, two attributes offer redemption: when a biotech is successful it can provide stellar returns, and the majority of biotechs deliver a socially significant and beneficial impact. Both of these characteristics appeal to the high net worth investor, and as such there is a place for biotech in this corner of their portfolio.

The EIS venture capital scheme helps mitigate some of the risk and eases the investor into the field. The scheme could go further in this mission, but at present it offers one of the most valuable investment avenues for the early-stage biotech industry in the UK. EIS support has provided the majority of Touchlight’s funding, and with it we employ over 20 scientists, have developed a robust platform, and are now commercialising and monetising our technology. The EIS scheme will continue to play an important role in funding an industry that is working hard to build market appetite for patient and forward thinking investment.

“The EIS scheme will continue to play an important role in funding an industry that is working hard to build market appetite for patient and forward thinking investment.”
Dealmaking

M&A

During 2015 M&A activity was not entirely dominated by the industry’s big players. While Shire – the largest cap company in our analysis – did account for the biggest acquisition of the year, relatively newly-listed companies such as Circassia and Clinigen held their own. The two companies both managed to pull off £100m plus deals. Continued consolidation in the specialty pharma space saw Alliance Pharma buy Sinclair Pharma’s healthcare products business and Clinigen take out LINK Healthcare. The desire to diversify was behind Circassia’s acquisition of Prosonix.

Conversely, rising valuations and favourable capital markets all helped the UK companies putting themselves up for sale achieve healthy returns for their investors. The fevered market for speciality pharma assets paid off for Amdipharma, which came out of stealth mode with its £2.31bn sale to Concordia Healthcare. Other notable sales were Sosei’s acquisition of Heptares.

The view in 2016

A key move to note in 2016 is the £441m merger between UK-listed companies Vectura and Skypharma, to create a world leader in the respiratory field.

Although their size excludes them from our analysis, it’s important to mention the collapse of Pfizer and Allergan’s merger, following changes to tax inversion rules in the US. Could this signal the start of a decline in biopharma mega deals and perhaps more opportunities for smaller companies as we enter the second half of the year?

Key M&A activity, UK companies acquiring, 2015

<table>
<thead>
<tr>
<th>Company</th>
<th>Country</th>
<th>Acquired or merged company</th>
<th>Country</th>
<th>Total (£m)</th>
<th>CVRs/milestones (£m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shire</td>
<td>UK</td>
<td>NPS Pharmaceuticals</td>
<td>USA</td>
<td>3377.2</td>
<td>-</td>
</tr>
<tr>
<td>Shire</td>
<td>UK</td>
<td>Foresight Biotherapeutics</td>
<td>USA</td>
<td>192.3</td>
<td>-</td>
</tr>
<tr>
<td>Alliance Pharma</td>
<td>UK</td>
<td>Healthcare Products (non-aesthetics)</td>
<td>UK</td>
<td>132.2</td>
<td>-</td>
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<tr>
<td>Circassia</td>
<td>UK</td>
<td>Prosonix</td>
<td>UK</td>
<td>100.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Clinigen Group</td>
<td>UK</td>
<td>LINK Healthcare</td>
<td>Australia</td>
<td>100.0</td>
<td>55.5</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®

Note: excludes mega-cap companies such as AstraZeneca and GlaxoSmithKline
### Key M&A activity, UK companies acquired, 2015

<table>
<thead>
<tr>
<th>Company</th>
<th>Country</th>
<th>Acquired or merged company</th>
<th>Country</th>
<th>Total (£m)</th>
<th>CVRs/ milestones (£m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordia Healthcare</td>
<td>Canada</td>
<td>Amdipharm Mercury Company</td>
<td>UK</td>
<td>2309.5</td>
<td>144.0</td>
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<tr>
<td>Biogen</td>
<td>USA</td>
<td>Convergence Pharmaceuticals</td>
<td>UK</td>
<td>445.0</td>
<td>313.2</td>
</tr>
<tr>
<td>Allergan</td>
<td>Ireland</td>
<td>Auden Mckenzie</td>
<td>UK</td>
<td>306.0</td>
<td>-</td>
</tr>
<tr>
<td>Sosei</td>
<td>Japan</td>
<td>Heptares Therapeutics</td>
<td>UK</td>
<td>258.6</td>
<td>142.3</td>
</tr>
<tr>
<td>Ipsen</td>
<td>France</td>
<td>Canbex Therapeutics</td>
<td>UK</td>
<td>72.2</td>
<td>66.2</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®

Note: excludes mega-cap companies such as AstraZeneca and GlaxoSmithKline

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**Malcolm Weir, CEO, Heptares Therapeutics**

Sosei’s acquisition of Heptares in March 2015 has been a successful transaction for all parties. It was the result of Sosei’s approach to Heptares, following its global search for an M&A target with a powerful discovery platform capable of creating a sustainable pipeline of high value therapeutic candidates, and the promise of near-term deal-flow from partnering of pre-existing pipeline and platform. The latter has paid off handsomely in the shape of deals with Allergan, AstraZeneca, Teva, Pfizer and others totalling over $175m up-front cash and premium equity and over $6bn in potential milestones plus royalties. This has been reflected in a step change in the Sosei Group share price (listed in Japan), as well as earn-out payments to former Heptares’ shareholders.

Critically, and connected to the validation these deals bring, Sosei is making Heptares the focus of its future expansion, bringing inward investment to the UK in research, translational medicine and clinical development.

This company-building outcome for Heptares compared highly favourably with other viable alternatives such as further private rounds, purely asset-driven acquisition without commitment to the platform, or listing on a public market. Heptares had reached the milestone of being a clinical-stage company, at which point the need to access substantial further capital to progress its clinical candidates through proof of concept became pressing, and to do so via a supportive acquirer with an aligned business model was attractive.

“This company-building outcome for Heptares compared highly favourably with other viable alternatives”
The strengthening of the licensing market in 2014 continued into 2015, again fuelled by rising valuations and big companies’ desire to find innovative technology. The increased competition in the market was shown by the number of early-stage deals, including AstraZeneca’s potential £2.62bn deal for pre-clinical assets from Ionis Pharmaceuticals.

However, despite a desire to get in on the ground floor of innovation, big pharma companies were also sensibly hedging their bets and many early deals continued to be heavily back ended. The two research projects GlaxoSmithKline signed had only one disclosed upfront payment of £2m.

2015 might also be remembered as the year of outsourcing, as AstraZeneca and GlaxoSmithKline continued the trend among big pharma of disposing of non-core assets.

The view in 2016

The search by larger companies to unearth innovative technology from within the field of small biotech is a long-term trend and as such the licensing market is likely to continue to strengthen over the coming year – something the UK is well placed to reap the benefits from with its world renowned research base and the wealth of companies emerging from the IP commercialisation sector.

Following their acquisition by Sosei in 2015, Heptares have completed a number of notable deals in 2016, including their $3.3bn agreement with Allergan following the demise of its mega-merger with Pfizer.

The potential power of combination therapies also looks to be a key driver for partnering into 2016 and beyond.

Key partnering activity, UK companies, 2015

<table>
<thead>
<tr>
<th>Status of project on Deal Date</th>
<th>Company</th>
<th>Country</th>
<th>Deal Partner/Product Source</th>
<th>Country</th>
<th>Upfront Payment (£m)</th>
<th>Deal Value (£m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-clinical</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>Ionis Pharmaceuticals</td>
<td>US</td>
<td>42</td>
<td>2,621</td>
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<tr>
<td>Phase II</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>Innate Pharma</td>
<td>France</td>
<td>165</td>
<td>840</td>
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<tr>
<td>Phase II</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>Inovio Pharmaceuticals</td>
<td>US</td>
<td>18</td>
<td>468</td>
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<tr>
<td>Pre-clinical</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>Sosei</td>
<td>Japan</td>
<td>6</td>
<td>329</td>
</tr>
<tr>
<td>Research project</td>
<td>GlaxoSmithKline</td>
<td>UK</td>
<td>Zymeworks</td>
<td>Canada</td>
<td>-</td>
<td>292</td>
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<tr>
<td>Phase III</td>
<td>EUSA Pharma</td>
<td>UK</td>
<td>AVEO Oncology</td>
<td>USA</td>
<td>2</td>
<td>266</td>
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<tr>
<td>Pre-clinical</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>Eolas Therapeutics</td>
<td>USA</td>
<td>-</td>
<td>92</td>
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<tr>
<td>Research project</td>
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<td>UK</td>
<td>Orca Pharmaceuticals</td>
<td>UK</td>
<td>-</td>
<td>79</td>
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<tr>
<td>Research project</td>
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<td>UK</td>
<td>Idera Pharmaceuticals</td>
<td>USA</td>
<td>2</td>
<td>68</td>
</tr>
<tr>
<td>Phase II</td>
<td>Tiziana Life Sciences</td>
<td>UK</td>
<td>Nerviano Medical Sciences</td>
<td>Italy</td>
<td>2</td>
<td>28</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®. Only partnerships where value disclosed.
### Key partnering activity, UK companies, 2015

<table>
<thead>
<tr>
<th>Status of project on Deal Date</th>
<th>Company</th>
<th>Country</th>
<th>Deal Partner/Product Source</th>
<th>Country</th>
<th>Upfront Payment (£m)</th>
<th>Deal Value (£m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase III</td>
<td>Novartis</td>
<td>Switzerland</td>
<td>GlaxoSmithKline</td>
<td>UK</td>
<td>191</td>
<td>659</td>
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<tr>
<td>Approved</td>
<td>Daiichi Sankyo</td>
<td>Japan</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>136</td>
<td>560</td>
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<td>Research project</td>
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<td>USA</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>291</td>
<td>291</td>
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<tr>
<td>Phase III</td>
<td>Valeant Pharmaceuticals International</td>
<td>Canada</td>
<td>AstraZeneca</td>
<td>UK</td>
<td>65</td>
<td>290</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®, Only partnerships where value disclosed

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**Shaun Grady, Vice President, Business Development Operations, AstraZeneca**

The increasing mix between licensing and partnership agreements alongside more traditional M&A illustrates the increasingly embedded focus across the industry on collaboration, no longer as ‘nice-to-haves’ but as an integral and necessary part of discovering and developing the next generation of innovative medicines.

AstraZeneca’s pattern of deal-making in 2015, but also in recent years, is no different, and there are significant benefits to collaborations, bringing together different strengths, capabilities and expertise to test new hypotheses, and share cost and risk to maximise the potential of molecules for the ultimate benefit of patients.

AstraZeneca-MedImmune signed a number of exciting licensing and partnership agreements in 2015, driven by our strategy of making smart additions to and gaining greatest value from our portfolio and pipeline in our main therapy areas. Importantly, this work is also being guided by an increasing focus on combination treatments, unlocking their potential to target areas of real unmet patient need.

We concluded a collaboration with Innate Pharma to broaden the development of their anti-NKG2A antibody across a range of solid tumours, including in combination with our anti-PD-L1 immune checkpoint inhibitor durvalumab. We also signed licensing agreements with Lilly, Mirati Therapeutics and Peregrine among others, to explore novel combinations of our immunotherapies and small molecules in different cancers.

Licensing and collaboration agreements like these allow us to test the potential of new combinations enabling us to then follow the science in terms of future trial design and deal structure. We’re really only starting to get to grips with the full potential of what can be achieved from partnering to combine novel therapies. I can only see this trend continuing across the sector into 2016 and beyond.

“We’re really only starting to get to grips with the full potential of what can be achieved from partnering to combine novel therapies”
Pipeline and approvals

The UK remains an R&D powerhouse, with the 585 pipeline projects in development far outstripping other European countries. Nearest rival France has 466 products. The UK also leads the way with late stage drugs, with 51 Phase 3 projects compared with 42 for France and 40 for Switzerland.

The rate of both US and European approvals for UK companies is also well ahead of European peers. Despite its smaller number of biotech companies the UK reported more regulatory wins than Massachusetts and only just fell short of the 16 FDA approvals reported by Californian companies. The tally was helped by contributions from both the UK’s new and established companies including Vectura’s Seebi Neohaler, Abzena’s Cosentyx and BTG’s Anavip.

The view in 2016

So far in 2016 we have seen pivotal Phase 3 trial results from GW Pharma, which led to a surge in the company’s share price. We also await the results of Circassia’s lead programme, targeting cat allergy, on track to report Phase 3 results in Q2 2016.

Therapeutic pipeline by phase for leading European biotech hubs, 2015

![Therapeutic pipeline chart](chart_url)
**EMA and FDA approvals from leading European and US biotech hubs, 2015**

<table>
<thead>
<tr>
<th>Country</th>
<th>EMA Approvals</th>
<th>FDA Approvals</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>France</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Germany</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Switzerland</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>California</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>2</td>
<td>7</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma®. Excludes companies with a market cap above $40bn.

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**Justin Gover, Chief Executive Officer, GW Pharmaceuticals**

The positive outcome of our first Phase 3 trial in Dravet syndrome is a significant milestone in the development of Epidiolex as a potential new treatment for patients suffering with this very difficult condition. We are excited about the potential for Epidiolex to become the first FDA approved treatment option specifically for Dravet syndrome patients and their families.

Following these positive results, GW is now entering an exciting new chapter as we start to prepare the company’s first NDA submission to the FDA and step up plans for Epidiolex commercialisation.

The robust data from this first Phase 3 trial in Dravet syndrome provides additional confidence for future clinical trials of Epidiolex and we look forward to results from our Phase 3 trials in Lennox-Gastaut syndrome in the near future. In addition, we continue to expand our research through exploring further indications for Epidiolex as well as ongoing Phase 2 clinical programs for a number of our pipeline candidates.

“Following these positive results, GW is now entering an exciting new chapter as we start to prepare the company’s first NDA submission to the FDA and step up plans for Epidiolex commercialisation.”

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**The view in 2016**

Over the past couple of years we have seen the development of new regulatory pathways, designed to accelerate access to the innovative new medicines we see in development across the sector.

New for 2016 was the launch of the EMA’s priority medicines scheme, or PRIME, modelled on the FDA’s breakthrough therapy designation.
The BIA would like to thank Evaluate and the London Stock Exchange for providing the data contained within this report and for their expertise. The BIA are also extremely grateful to all those who have provided insightful commentary pieces for this report.

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Unless stated otherwise, £m valuation is derived from exchange rates on the financing date.

The average annual exchange rates used are detailed below (US$/UK£):

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>0.647</td>
</tr>
<tr>
<td>2011</td>
<td>0.624</td>
</tr>
<tr>
<td>2012</td>
<td>0.631</td>
</tr>
<tr>
<td>2013</td>
<td>0.639</td>
</tr>
<tr>
<td>2014</td>
<td>0.607</td>
</tr>
<tr>
<td>2015</td>
<td>0.654</td>
</tr>
</tbody>
</table>

Unless stated otherwise, data excludes companies with market cap above $20bn
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