UK BioIndustry Association

TechBio 2023

UK driving the AI revolution

In collaboration with

CITELINE
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Contents

Forewords

Steve Bates OBE,
CEO, BIA

TechBio is the interface where life science and artificial intelligence (AI) meet. TechBio companies helping to develop new drugs and therapies more quickly, personalising and targeting medicine more accurately, creating powerful new diagnostic tools, and improving the end-to-end efficiency of discovery in the life sciences. These innovations have the potential to improve the health and well-being of people around the world and to speed up potential solutions to global sustainability challenges.

The BIA is committed to supporting the growth of the TechBio sector and to raising awareness of the companies in this space and their incredible potential. It is a sustainable competitive advantage for the UK. Across both financings and alliances, the UK is second only to the US for TechBio deal-making over the last 18 months.

Over the past few years, we have been on a journey with our developing TechBio community, providing great events and networking, sector promotion and guidance. The BIA is also working hard to advocate on issues our members have told us matter to them:

- Access to data for SMEs and development of coherent UK health data infrastructure
- Developing a pool of digital and data-focussed talent
- Access to greater multiples of investment to enable sustainable and patient funding of scaling TechBio companies in the UK
- Development of appropriate and proportionate regulatory frameworks to both enable and harness innovation for good.

Building on our first report, TechBio: How data-driven life sciences companies are transforming drug discovery and patient care and our second report, TechBio 2.0: Unlocking Data, Transforming Biology, activity in this part of the sector has continued at pace. In this third TechBio report, we revisit progress in these areas, take a bird's eye view of the broader state of TechBio as the sector matures, and highlight some incredible new companies in the space.

I would like to thank Luca Parisi (Director, Clinical Analytics and Data Science, Citeline), Daniel Chancellor (Director, Thought Leadership and Consulting, Citeline), and James Wong (Venture Partner, MedTech SuperConnector, Expert-in-Residence, Imperial College London and BIA TechBio UK Advisory Group) for contributing to the report.

TechBio involves a paradigm shift from a science-first to a technology-first approach throughout the continuum of drug discovery, development, clinical trial planning and execution, and drug repurposing.

Luca Parisi, PhD, MBA
Director, Clinical Analytics and Data Science, Citeline

At every step in the drug development pipeline and clinical trial lifecycle, data science and AI, combined with scientific and clinical expertise, have already demonstrated significant added value. Early examples of this include BenevolentAI's record-time repurposing of drugs from rheumatoid arthritis to COVID-19, and with InSilico Medicine's discovery of a new small molecule, entirely generated by AI, to treat idiopathic pulmonary fibrosis.

We believe the evolution of the TechBio community will impact the broader life sciences industry in a critical way and even may become a competitive necessity. TechBio will be an integrated, crucial link within the biotech world, where the borders will soon begin to blur. Thus, at Citeline, we are working hard to leverage data science and AI-driven solutions to support clients throughout the clinical trial lifecycle in:

- Protocol design and optimisation
- Trial feasibility
- Country, site, and investigator selection
- Patient education, engagement, and recruitment
- Streamlining disclosure.

I would like to thank Steve Bates and the BIA team for the opportunity to contribute to this report and communicate the value that the TechBio community provides, both globally and here in the UK.

The big picture for TechBio

UK TechBio is fast emerging - beyond the core definition of AI applied in drug discovery, design and development, there is a broader spectrum of frontier technologies, platforms and tools to improve clinical decision-making, workflow productivity and cost savings.

James Wong
Venture Partner, MedTech SuperConnector
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BIA TechBio UK Advisory Group

TechBio teams work across scientific disciplines - from machine learning (ML) and robotics to engineering biology and genomics - applied to solve R&D and industrial challenges in biotech, pharma and healthcare delivery (for example, from the computational discovery and design of small molecules and antibodies to multi-omics clinical pathways). The platforms and tools developed may also be applied in other industries. For example, in addition to biotech, InstaDeep's AI-enabled decision-making solutions have also been applied in diverse industries, including in the technology, transport and logistics, industrial, and financial services sectors. InstaDeep has since been acquired by BioNTech to support the listed company's strategy of building capabilities in AI-driven drug discovery and development of immunotherapies and vaccines.

As we are seeing from the innovative startups featured in this TechBio report, there is value created in the platforms and tools being developed by multi-disciplinary teams, potentially offering multiple shots on goal to generate a pipeline of products (for example, therapeutic platform startups have the option to advance select assets to the clinic independently and co-develop with external industry partners, further realising value with upfront and milestone-driven payments). This contrasts with traditional asset-focused biotech models and seeks to mitigate binary, all-or-nothing outcomes, a key reason why investors are being drawn to TechBio as an emerging sector.

While there is a growing number of local and global investors at the intersection of technology and life sciences, co-investing in UK TechBio, there are differing investment strategies, attitudes to risks and returns, as well as preferences on how a startup should develop and scaleup. CEOs should therefore build investor

syndicates aligned on expectations in value creation, valuation and exit, and in parallel explore collaboration and partnering with academia and industry to strengthen their access to resources, from drug discovery to applied computing. Early-stage innovators should also explore how best to leverage other funding sources such as grants.

The UK has long been recognised as a leading source of academic research and innovation across AI, genomics and synthetic biology - this is now increasingly being translated into a source of spinout and startup activity. As featured in the first edition of the UK TechBio Landscape, which illustrated the variety of category-defining companies in the UK, there have been new companies created such as Isomorphic Labs, led by DeepMind co-founder and CEO, Demis Hassabis, who having achieved a proof point in AlphaFold, believes the timing for AI in drug discovery has arrived.

From capital, talent and space to data, skills and policy, the BIA has a key role to play in ensuring that the momentum in data-driven discovery in life sciences continues, raising awareness of both the opportunities and challenges of this emerging sector, celebrating the success stories of innovators and bringing together our industry.

The annual state of TechBio

Authored by Luca Parisi and Daniel Chancellor, Citeline.

These are exciting times for the TechBio community, from the pioneering start-ups and academics through to their industry partners and investors. Generative AI has now become part of everyday conversation through the success of ChatGPT and others, raising awareness of some of the tools that underpin the technology aspect of TechBio companies. Meanwhile, biotech drug pipelines are as deep as ever with the validation of new modalities and patient data being generated at pace. For those companies operating at this interface, the use cases are maturing rapidly with real-world examples. We believe the evolution of the TechBio community will impact the broader life sciences industry in a critical way and even may become a competitive necessity.

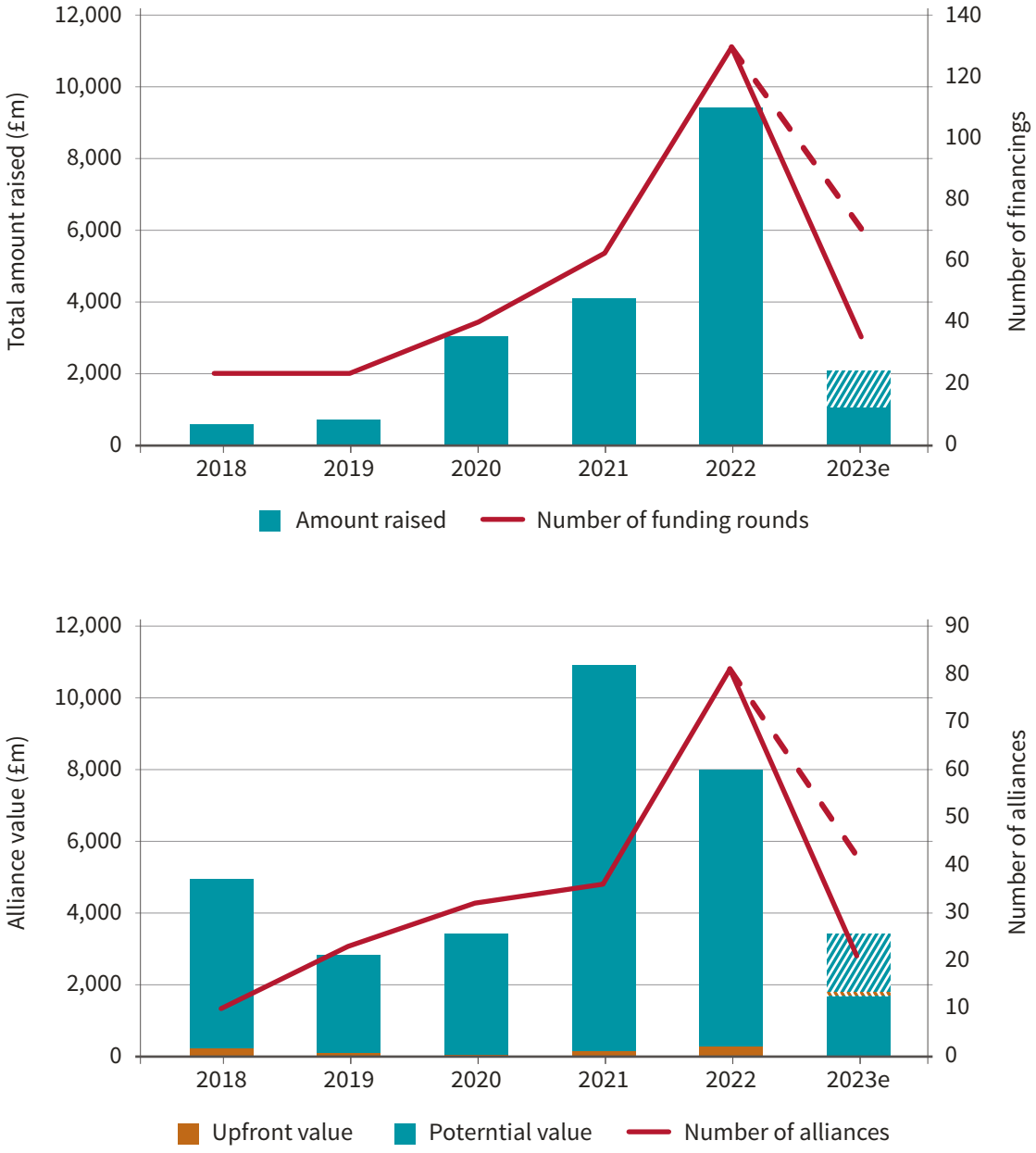
This includes AI-driven drug discovery, whereby algorithms are enabling the design and optimisation of novel small molecules and proteins with accuracy and scale that conventional drug discovery cannot match. Furthermore, existing treatments can be repurposed using AI-derived biological insights, with multi-factorial matching of patients to clinical trials that are designed to maximise the likelihood of success. Such processes will expedite the overall R&D process and drug development pipeline, lowering the degree of attrition during late-stage clinical trials, and thus addressing key industry productivity challenges.

Furthermore, expansion and integration of patient data into early R&D decision-making will be transformational for the future of healthcare. The broad adoption of multi-omics tools is generating new insights into fundamental human biology and precision medicine. Diseases are increasingly viewed as a function of such biomarkers, along with other complementary data, such as form both ionising and non-ionising, functional and morphological medical imaging, which ultimately guide diagnosis, treatment, and connected care in the real-world setting.

The cost and complexity of drug development requires experienced and committed partners. Therefore, the long-term success of TechBio is dependent upon the flow of investment and alliances with mature life sciences companies. This collaborative model, long established between big pharma and emerging biotechs, has proven many times over an ideal framework to develop new treatment options for patients. The broader state of TechBio can therefore be gauged through such deal-making activity.

It is difficult to capture the totality and nuance of TechBio – which sits at the intersection of many different disciplines – within any standard industry dataset. Citeline tracks global deal-making activity in life sciences and assigns an AI classification to companies and deals where relevant, which can be used as a proxy for the TechBio universe. The charts below summarise total financing and partnership activities involving AI.

Figure 1. Growth in global TechBio financing and partnering activities



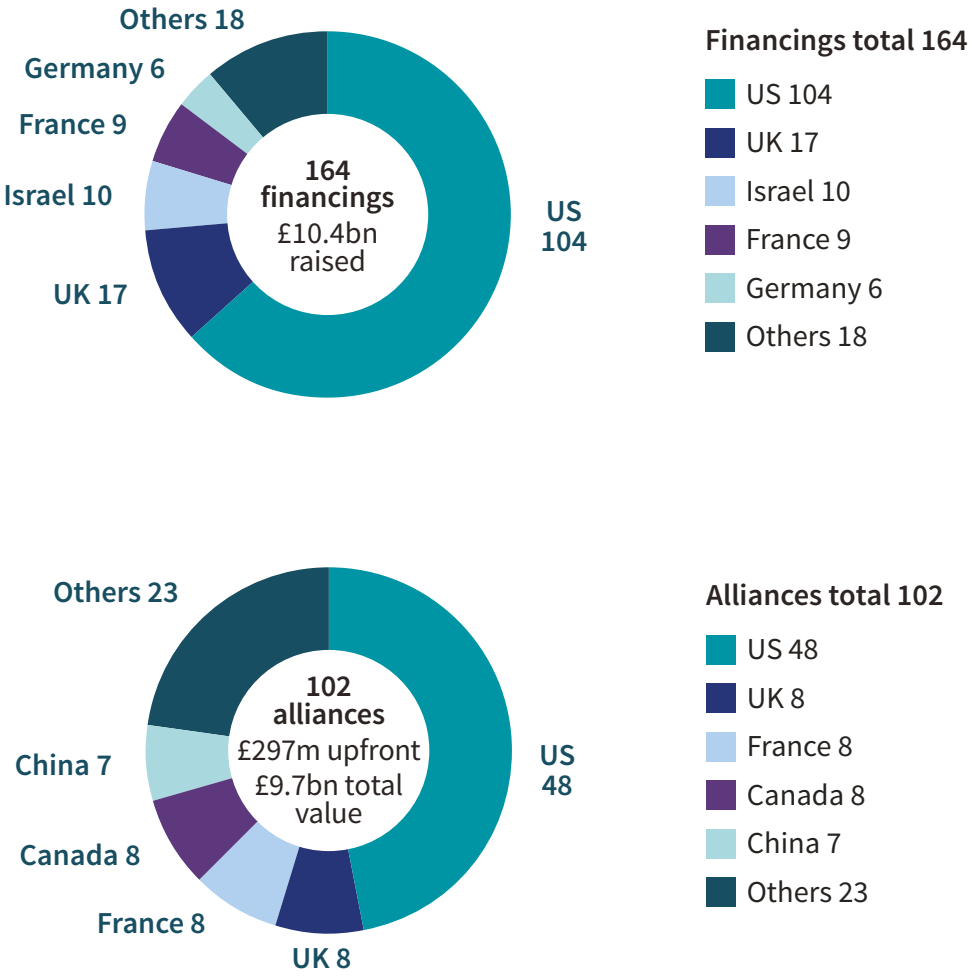
Source: Biomedtracker, July 2023

It is somewhat of an understatement to say that TechBio deal-making is on the rise. Life sciences companies raised a record £9.4 billion investment in 2022 to further advance their AI platforms and assets, with this total having doubled every year since 2018. The number of alliances with biopharma partners is also following a similar trajectory, although their value is rather more volatile and heavily swayed by milestone components. Nevertheless, £263 million in upfront payments was a record for 2022, spread across 81 separate partnerships.

The first half of 2023 has not been able to sustain the incredible amount of global activity within 2022. Speaking to Citeline's In Vivo, Ivan Griffin of BenevolentAI explained: ***"Investment and growth have slowed down and people are waiting to see critical readouts and data that validate the thesis that AI can significantly benefit drug discovery and reduce attrition."***

Deal values and volumes are down sharply as TechBio has not been immune to broader market uncertainties, although the UK has been an outlier. Here, TechBio companies are on track to exceed last year's £161 million in fundraising across 10 deals, with seven financings bringing in a total of £87 million so far in 2023. This resilience is enabling the UK TechBio ecosystem to secure a prominent position in the global rankings. Across both financings and alliances, the UK is second only to the US for TechBio deal-making over the last 18 months.

Figure 2. Global TechBio financing and partnering activity by geography, 2022 to 2023 Q2



Source: Biomedtracker, July 2023

UK companies driving the AI revolution

The UK TechBio ecosystem contains a range of different technologies and business models. Companies such as Exscientia and BenevolentAI are at the vanguard, becoming fully-fledged biotechs with a blend of strategic alliances, such as multi-year strategic partnerships between BenevolentAI and AstraZeneca, out-licensed assets, and internal drug pipelines. Several others are bidding to make the transition from discovery science to clinical-stage candidate. Earlier on the lifecycle, there are a range of venture capital-backed service providers with specific capabilities in a particular R&D step, therapy area or diagnostic tool. Some of the key milestones of these companies so far in 2023 include:

Exscientia

Exscientia continues to make clinical progress

Having raised close to $500 million (~£360 million) from investors during its 2021 initial public offering (IPO) and private placement, Exscientia has now progressed six assets into clinical trials, either through strategic alliances or as internal R&D programs. Three of these are under development by Sumitomo Pharma for CNS disorders, while the remaining programs target cancer and inflammatory diseases. Of note, the ELUCIDATE basket trial of a CDK7 inhibitor is now underway, with broad potential application in a range of prevalent solid tumours. Exscientia also regained control of assets discovered in collaboration with Bristol Myers Squibb against the complex cancer targets LSD1 and MALT1.

BenevolentAI

BenevolentAI announces Phase II data for lead asset in atopic dermatitis

Demonstrating the progress of the first AI-discovered assets through the pipeline, BenevolentAI released top-line data for its candidate BEN-2293 for the treatment of atopic dermatitis. The study met its primary endpoint, showing safety and tolerability, although secondary endpoints for efficacy were not reached. BEN-2293 failed to demonstrate a significant reduction in itch and inflammation over placebo, despite additional analyses suggesting a positive treatment effect in more severely affected patients. BEN-2293 acts as a Trk inhibitor, more commonly known as a mechanism for cancer, but with potential in immunology conditions, as suggested by BenevolentAI's platform.

Charm Therapeutics secures BMS alliance and funding from Nvidia

London-based Charm Therapeutics is one of the few TechBios to secure financing so far in 2023. New investment from Nvidia raises total fundraising to date of $70 million (£56 million) and adds to an already impressive syndicate of venture capital firms. This investment will further fuel the development of Charm's DragonFold platform which can identify novel molecules through protein-ligand co-folding. In addition, Charm secured its first industry partner in Bristol Myers Squibb, leveraging DragonFold to discover novel molecules against targets of interest. BMS is then able to exercise options to license and develop any compounds that arise from this collaboration.

Perspectum completes $55 million Series C round

Representing the diagnostics angle, Perspectum, a University of Oxford spinout collaborating with the Microsoft company 'Nuance Communications', secured the largest investment for a UK TechBio during H1 2023. The company raised $55 million (£44 million) during its Series C round, bringing the total amount since inception to ~$140 million (~£110 million). With this injection, Perspectum is advancing tools to improve the diagnoses of metabolic diseases and cancer, including its commercially available LiverMultiScan. Perspectum's core AI software enhances the capabilities of non-invasive, non-ionising MRI, allowing a denoised capture of multiparametric data and the volumetric measurement of organ inflammation, enabling more data-informed and precise diagnosis.

BIOS Health plugs into new investment for AI-powered neural interfaces

Also bucking the broader biotech downturn, BIOS Health received new funding from a range of investors, including the TechBio fund Selvedge Venture. BIOS Health is a pioneer in combining AI technologies and precision neurology and is providing its capabilities to the US NIH as part of the REVEAL study. The ambition is to sequence neural biomarkers to elucidate the link to various disease states, much as genetic sequencing has resulted in significant breakthroughs for drug discovery in cancer and rare diseases.

TechBio innovation showcase

We take a closer look at six incredible earlier stage BIA member companies driving innovation in the TechBio space.

Case study

BRAINOMIX

What does the company do?

Brainomix specialises in the creation of AI-powered software solutions to enable precision medicine for better treatment decisions in stroke and lung fibrosis. With origins as a spin-out from the University of Oxford, Brainomix is an expanding commercial-stage company that has innovated award-winning imaging biomarkers and software solutions that are used in more than 30 countries worldwide.

How does the technology work?

Brainomix's flagship product, the 360 Stroke platform, is a collection of tools that use state-of-the-art AI algorithms to support doctors by providing real-time interpretation of brain scans to help guide treatment and transfer decisions for stroke patients, allowing more patients to get the right treatment, in the right place, at the right time.

A recent study found that the implementation of the 360 Stroke platform enabled faster treatment, reducing the door-in-door-out (DIDO) time by more than one hour from 140 to 79 minutes. More importantly, the study also found that the rate of patients achieving functional independence (mRS 0-2 @ 90 days) trebled, from 16% to 48%.

As a result of an NHS AI grant that Brainominx were awarded in September 2020, they were able to deploy the 360 Stroke platform across five networks in the UK. Recent data collected by the Oxford Academic Health Science Network found that the sites that had adopted Brainomix 360 Stroke platform had a significantly higher rate of thrombectomy, a life-changing treatment which can reduce disability and prevent or limit long-term care needs in patients with the most severe strokes.

How will it be used?

The Brainomix 360 Stroke platform is seamlessly integrated into a stroke network, automatically processing any brain scans ordered as part of the stroke imaging protocol, and then generating AI-derived outputs that help a physician decide the best course of treatment. The Brainomix 360 platform is the most comprehensive stroke AI imaging platform, supporting all levels of imaging needs across the network.

What are the opportunities and challenges?

Brainomix's greatest opportunity in the near term is to expand its commercial operations into the US market. They are currently market leaders in Europe, with some impressive recent milestones, including a national-level deployment of software across all 36 Hungarian stroke centres, as well as winning the Welsh national tender. Brainomix are looking to leverage this success and experience into the US market, which remains the most lucrative market globally, but with fierce competition from companies such as RapidAI and Viz.ai.

In terms of challenges, like all other AI companies, are facing growing scepticism – and, in some cases, even distress – about the role and value of AI, but Brainomix believe that there is growing real-world evidence to demonstrate the value of their technology in stroke.

Case study

CardiaTec

What does the company do?

CardiaTec is the first AI-enabled drug target discovery company specialised in cardiovascular disease, the leading cause of death globally. Its human-centric, multi-omics approach allows for the identification of novel and better biologically defined drug targets with an increased probability of clinical success.

How does the technology work?

CardiaTec is building the first and largest proprietary multi-omics dataset of human cardiac tissue. This platform integrates various biological data layers, including genomics, transcriptomics, epigenomics, and proteomics, to provide a comprehensive understanding of disease biology. By employing advanced AI algorithms, CardiaTec identifies and prioritises dysregulated drug targets and disease-related pathways. This approach enables the discovery of drug targets with well-defined mechanisms of action that are causal of disease thereby increasing the likelihood of successful clinical translation.

How will it be used?

CardiaTec's initial focus is on coronary artery disease. The platform has incorporated multi-omics data from coronary tissues. Unlike traditional targeted omics data analysis and hypothesis-driven drug target discovery, CardiaTec's model employs a fully unbiased multi-omics approach. This enables the models to suggest new pathways and proteins without being influenced by current knowledge or scientific expectations. This approach fosters the discovery of entirely novel pathways that might not have been previously considered in the development of therapeutics for coronary artery disease.

What are the opportunities and challenges?

Challenges in cardiovascular disease space:

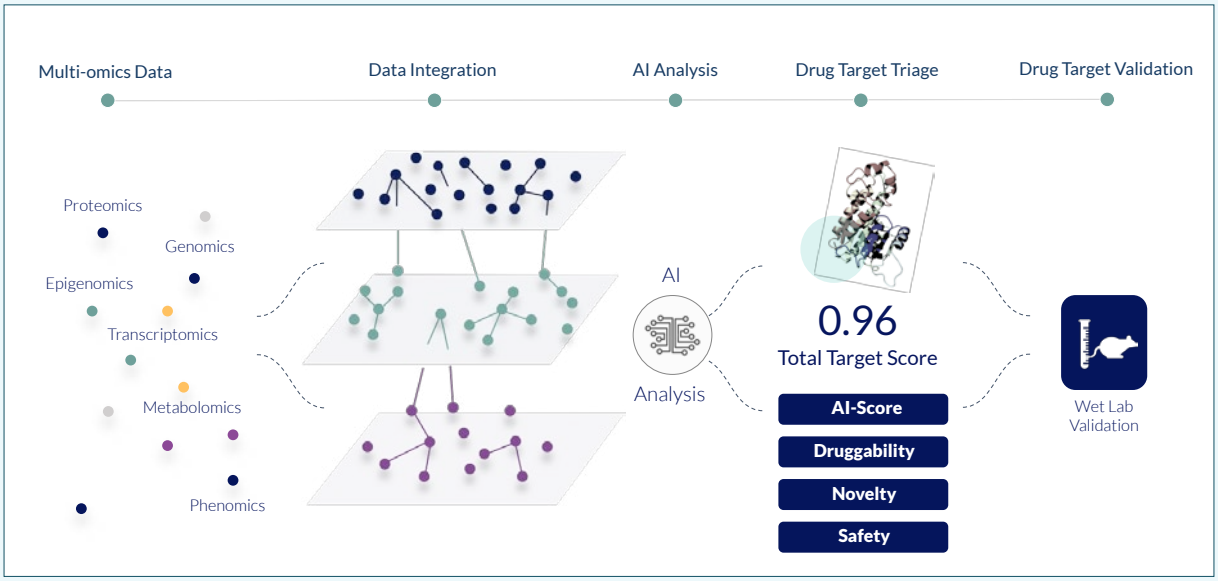
- Cardiovascular disease is the leading cause of death globally, yet therapeutic innovation has been stagnant. The drug development pipeline for cardiovascular disease has experienced minimal growth in the last 10 years compared to other therapeutic areas despite the high mortality rate
- The complexity and multifactorial nature of cardiovascular disease pose significant challenges in understanding its underlying pathophysiology. Current investigative techniques, such as single omics analysis, provide a limited understanding of disease mechanisms, impeding the identification of effective drug targets. Consequently, the clinical translation of associated drugs has been suboptimal, leaving a substantial unmet need for more effective treatments.

Opportunities:

- Cardiovascular disease represents a significant global health concern, offering a substantial market for innovative therapies
- There's potential for substantial advancements in drug development for cardiovascular disease, considering the relatively stagnant progress in recent years
- The emergence of more comprehensive technologies, including multi-omics, allows for the complexity of cardiovascular biology to be better captured.

What are the future trends?

CardiaTec plans to expand its multi-omics data generation and drug target discovery to encompass additional cardiovascular indications in the future.



Sixfold.

What does the company do?

Sixfold Bioscience is a biotechnology company solving one of the most critical challenges preventing the greater utilisation of RNA therapeutics: delivery. From their West London labs, the team of fewer than 25 biologists, chemists, automation engineers and computer scientists have built an RNA delivery platform that combines evolution's ability to solve highly complex problems with the speed of computation.

How does the technology work?

Sixfold's solution takes evolution as inspiration, learning and mimicking how RNA is naturally delivered to different cell types in the body. Their proprietary RNA-based tagging system, called Mergo®, co-opts the body's evolved shuttles that move RNA between cells as part of natural processes, delivering the therapeutic RNA cargo molecules to specific cell types beyond the liver. Using advanced AI/ML and high-throughput in vivo screens, Sixfold is learning the language that encodes RNA-shuttle interactions and destination selection, unlocking new cell types for treatment.

How will it be used?

RNA development is slightly different to that of traditional biologics or small molecule drugs. You need both a delivery system and a therapeutic; without effective in vivo delivery the therapeutic is useless. Alnylam Pharmaceuticals – the first to unlock the delivery of siRNA to one cell in the liver – were spending >80% of their R&D budget on RNA delivery, which they capitalised on to build a company with a market cap of >$20 billion. Sixfold's technology is applicable to multiple cell types beyond the liver, and the company sees Mergo® as an enabling technology that will catalyse the shift from potential to reality for RNA medicines, including siRNA and ASO.

What are the opportunities and challenges?

RNA's potential is vast but its reality is currently limited due to the fact that current delivery modalities can only target less than 2% of the ~500 human types cells. This presents a phenomenal opportunity for any company that can engineer targeted RNA delivery systems. However, the problem is highly complex, involving multiple biological barriers that are poorly characterised – the only way to know you have solved delivery is by observing the desired readouts in a relevant in vivo context. The Sixfold team is overcoming this challenge by using their platform to build the largest dataset of delivery systems tested in vivo.

What are the future trends?

Solving RNA delivery unlocks value. The GalNac ligand added over $36 billion in value to the RNAi market space, and it only improved delivery to an already tractable organ (the liver). By expanding delivery capabilities to new cell types beyond the organ, Sixfold Bioscience is poised to open up entirely new applications, and markets, for RNAi therapeutics.

Case study

Turing Biosystems

What does the company do?

Turing Biosystems has created an interpretable AI platform to design and optimise drugs and treatments with the aim of reducing side effects in patients or improving efficacy. Blockbuster drugs in oncology usually take more than 10 years to develop and cost more than $1 billion. Yet, about 60% of patients do not respond to most oncology drugs and for the patients that do respond, side effects and adverse interactions between drugs are a major issue.

The Turing Biosystems platform can integrate many kinds of omics data, such as genomics, transcriptomics, metabolomics, imaging, blood data and clinical data from patients, and connect what can be detected in this data with known biological mechanisms, entities and clinical knowledge.

How does the technology work?

The platform is based on automated reasoning AI - a type of AI always interpretable by design. It is quite different from machine learning methods, which are used everywhere, and are incapable of providing sound and precise scientific reasoning supporting their outputs.

Automated reasoning is an advanced computer science method that is able to reason rigorously on scientific prior knowledge and real-world evidence data. So, they can be used

on big or small datasets, heterogeneous datasets, or in precision medicine contexts where there may be only one or a few patients.

Automated reasoning is novel in the life sciences. It has been successfully used in the aerospace and defence industry, for example, for the design of airplane control systems, and for software controlling nuclear reactors. It is able to predict and simulate all the possible adverse events that can happen in a complex critical system and find ways to avoid those adverse events so that the system meets its design goals at all times.

How will it be used?

The platform is used both by R&D teams and clinical trials teams in pharma companies and biotechs, and research clinicians in hospitals. Turing Biosystems works with research clinicians and academic collaborators that may have an ongoing clinical trial or groups of patients that are challenging the state of the art in medicine, seeking solutions to unmet needs.

The platform helps them to get the best possible understanding of the patient state, to relate their condition to known biological mechanisms in scientific prior knowledge and clinical experience, and to explore which treatments could be combined to achieve desired clinical outcomes, reduce adverse events and avoid potentially harmful drug interactions.

What are the opportunities and challenges?

The opportunities lie in the vast amounts of patient data now becoming available particularly multi-omics data.

A lot of machine learning-based approaches are used in pharma, but they are difficult to interpret. They provide patterns and/or classifications but are not capable of giving the biological mechanisms behind these patterns that would explain why these patients are classified in this way and why they are responding the way they do.

Increasingly pharma is becoming aware of such limitations. This is where Turing Biosystems come into play, providing companies with a type of AI which is interpretable by scientists and grounded on biological scientific knowledge. Not another Oracle or BLACKbox that just spits out an output.

Turing Biosystems see an exciting opportunity in spatial data and are now starting to work on imaging and spatial transcriptomics data in clinical trials. It is hugely beneficial to understand the biological mechanisms happening in a tissue in a spatial and dynamic way and at the same time challenging for most classical approaches, to get a good and actionable understanding of what happens in a tissue, such as a tumour, for example.

What are the future trends?

Turing Biosystems' focus is the immune system, immune-related diseases and immune-related side effects.

They see a lot of momentum across the pharma industry around immune-related diseases which are very complex and challenging, as they are multi-dimensional diseases, combining factors across many dimensions of biology. These challenges fit perfectly with the capabilities of their platform, which has been designed specifically to tackle these biological complexities.

Case study

What does the company do?

Etcembly uses the power of AI to discover, design and optimise safe, effective and diverse TCRs to make next-generation therapeutics.

Etcembly's EMLy™ discovery engine is the world's largest machine-learning immune health platform. It uses generative large language models (LLMs) similar to ChatGPT to rapidly predict, design and validate TCR candidates. EMLy scans hundreds of millions of TCR sequences then engineers them to achieve low pM affinity and eliminate cross-reactivity.

EMLy combines LLMs with classical physics-based simulations, exploiting the speed and parallelisation provided by GPU computing. It is built and runs on NVIDIA DGX A100 and H100 systems, and the software has its roots in open software projects such as GROMACS for classical molecular dynamics and PyTorch for deep learning.

How will it be used?

T cell receptors (TCRs) are molecules on the surface of a type of immune cell known as a T cell. They recognise fragments of faulty or harmful proteins presented by cells via HLA receptors, targeting the cells for destruction by the immune system.

Unlike antibody-based immunotherapy approaches that only attack targets on the outside of cells, TCRs 'see' targets inside cells by recognising fragments of these internal proteins that are displayed on the cell surface.

Why are TCR-based therapeutics so exciting? TCRs are highly engineerable and have huge potential as therapeutics for cancer, autoimmune conditions, immunodeficiencies and more. The first TCR therapeutic, Immunocore's KIMMTRAK® for metastatic uveal melanoma, was approved by the FDA in 2022.

TCRs can also be used as biomarkers to identify patients with particular characteristics - for example, certain TCR sequences are more common in children who have a severe inflammatory response to COVID-19 infection.

Searching through huge databases of TCR sequences from many people reveals TCRs that recognise proteins of interest in a particular disease – for example, faulty molecules that are produced by cancer cells - which can be taken forward for development into a cell therapy or biotherapeutic. This is an incredibly slow and painstaking task, as there are millions of sequences to sift through and little information available about what makes a 'good' TCR.

What are the opportunities and challenges?

Every person has hundreds of millions of unique TCRs that reflect the immune history of pathogens they have been in contact with.

Searching through huge databases of TCR sequences from many people reveals TCRs that recognise proteins of interest in a particular disease – for example, faulty molecules that are produced by cancer cells - which can be taken forward for development into a cell therapy or biotherapeutic. This is an incredibly slow and painstaking task, as there are millions of sequences to sift through and little information available about what makes a 'good' TCR.

There are further problems once a target-binding TCR has been found. Natural TCRs tend to have low binding affinity to their targets, limiting their potency and effectiveness. They also have significantly high cross-reactivity, where the TCR recognises protein fragments on healthy cells as well as those on cancerous or other unhealthy cells. This can lead to side effects and safety issues.

Furthermore, current TCR-based therapies are specific for patients with a particular type of HLA (known as the HLA02 haplotype) that is usually found in people with European ancestry, limiting their use in global populations.

All these issues are major limitations in realising the potential of these game-changing therapies and making them more widely accessible to global markets.

What are the future trends?

Etcembly's rapid pipeline for discovery and optimisation unlocks the universe of TCRs, unleashing the potential of these powerful therapeutics to transform patient outcomes.

Further programmes include first-in-class assets against undisclosed targets in oncology and autoimmune disease, along with an immune engager targeting MAGE A4, which is present in several cancers including melanoma and non-small cell lung cancer.

The team is focusing on building partnerships with innovative biopharma companies working on next-generation immunotherapies as well as driving forward preclinical validation of its own pipeline of first-in-class TCR-based immune engagers.

Case study

SERNA BIO

What does the company do?

Serna Bio is working at the intersection of RNA biology, machine learning, and high throughput experimentation to build the world's first map of the druggable transcriptome to discover novel RNA targeting therapeutics.

Using this combination of computational tools, and novel high throughput in vitro assays, Serna Bio are writing the rule book to selectively and specifically target RNA structures. By harnessing the 70% of the human genome that transcribes to RNA, Serna Bio are expanding the target universe for new first-in-class therapeutics and aiming to treat complex diseases. Proteins, the focus of classical drug discovery encode only 2% of the human genome, while 70% of the human genome encodes RNA. While advances like AlphaFold are improving

understanding of proteins, the majority of the human genome, cannot be addressed with these tools. The tools to tackle RNA biology are still being developed. Advances like siRNA, and ASO, are being rapidly developed, yet still have delivery, manufacturing and cost challenges.

It is also possible to target RNA using the classical modality of small molecules, with a low cost of production and oral dosing. Yet, the tool kit to develop small molecules targeting RNA does not exist.

It is known that RNA can form a variety of secondary and tertiary structures, which are pivotal to its functions and post-transcriptional regulation. These structures can then be targeted for therapeutic development (Childs-Disney et al 2022). Initial work from Serna Bio (previously Ladder Therapeutics) has been published in collaboration with the NCI (Yazdani et al, 2023).

Targeting RNA instead of protein offers several advantages: it opens the door to new druggable targets and can downregulate or upregulate a protein of interest. Furthermore, it will enable us to target the "dark genome".

How will it be used?

Serna Bio's technology is used to develop new drugs and treatments for a variety of diseases, including cancer, rare diseases and infectious diseases.
In addition to these specific diseases, Serna Bio's technology is also being used to develop new drugs to treat a variety of other conditions, such as autoimmune diseases, neurodegenerative diseases, and cardiovascular diseases.

Serna Bio's technology is still in the early stages of development, but it has the potential to revolutionise the treatment of a wide range of diseases. By targeting RNA, the technology could be used to develop more effective and less toxic drugs, potentially also new drugs to address unmet needs.

What are the opportunities and challenges?

Talent is still being trained in silos. The industry requires interdisciplinary education where an engineer who wants to work in this domain needs to understand the difference between DNA and RNA and need to understand the difference between nucleus and cytoplasm. Unless someone makes that active choice at a young age, which they won't do if not exposed to it, there is no educational stream to bring on the skills and leadership that the sector needs.

TechBio companies need people who understand and can fluid fluently in their brain flip between Python and medicinal chemistry, and currently the education system is failing to provide the workforce equipped with these skillsets.

What are the future trends?

Serna Bio refers to itself as a data engineering company as opposed to an AI drug discovery company because data engineering has been the biggest challenge. Serna Bio have to generate large data sets and the future trends are going to focus on systematic, repeatable data generation and process monitoring.

Opportunities and challenges for UK TechBio

BIA Member companies give many reasons for choosing to be based in the UK. These include:

- Opportunities for NHS collaboration in research and development
- Government funding, including Innovate UK
- The breadth of excellent science coming out of UK academic institutions
- Access to science and technology talent
- Well-developed infrastructure
- Ties to Europe
- Growing public and private investor base
- The MHRA as a highly respected regulator
- Well-developed scientific clusters that attract international talent and innovation.

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They also cite the following new and ongoing challenges that require attention for the continued growth of the sector in the UK:

- Clarity on regulatory processes and innovative technologies such as AI
- Continuing shortage of skilled workforce at the interface of technology and biology
- Ongoing fragmentation of patient and health data in the UK, in spite of the NHS as a unique, national 'cradle to grave' public service
- Scaling up: TechBio companies require scaling, and patient capital in order to remain in the UK and flexible space that can accommodate and enable collaborative spaces
- Culture: bringing together a workforce that combines biological and computational expertise can create challenges of cohesion, communication and cultural norms.

Joined up thinking for data access

Data access is essential for TechBio companies. Companies can access data through a variety of sources and initiatives, including clinical trials, patient registries, and public databases. However, the quality and cost of data can vary depending on the source and data can be expensive and difficult for SMEs in particular to obtain.

In February 2023, the BIA, Association of Medical Research Charities (AMRC) and LifeArc organised a joint community event on facilitating collaborations for data access. The event was widely attended with participants providing a cross-sector view of the current aspirations of various stakeholders and the challenges faced in assembling and accessing high-quality patient datasets.

The initiative was designed to:

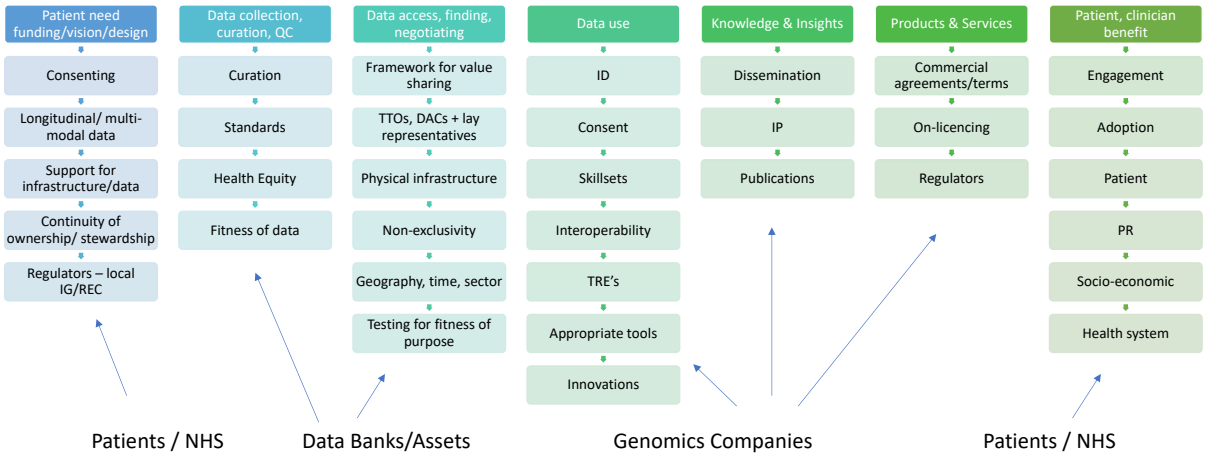
- Bring together industry, research charity and healthcare leadership to improve cross-sector understanding of the issues
- Set the scene for the data policy landscape
- Highlight examples of successful cross-sector data collaborations that are actively working on accessing, providing and using data
- Discuss further opportunities to address challenges.

Common issues raised focus especially on the practical challenges involved in enabling an efficient process of collaboration between diverse contributors to bring forward new research insights that are to the benefit of patients, the NHS and the wider UK life science and healthcare communities. The practical experience, challenges and best practices across all of the stages involved in data collection, access, use and exploitation were discussed from different perspectives:

- Study funders, Charities and Patients (AMRC, LifeArc)
- Universities (PQ) and TTOs (CC)
- NHS (HDR)
- SMEs (MS, BIA), biopharma and wider UK Government policy (BIA)
- Incubators and their start-up tenants (SBC)
- Commercial R&D Funders (Innovate UK).

The group discussed the various stages, contributors, challenges and best practices involved in building a successful collaboration and settled on a framework of key topics.

Issues identified



The circularity implied by a focus on the patient at the front and end of the framework is deliberate. It reflects the continual motivation and purpose of new research projects, the fundamental dependency on patients providing their data and samples, and also their key roles in realising the tangible benefits expected to accrue from any such R&D work. It is crucial to have enthusiastic, coordinated patient and clinician engagement to ensure that their data are captured accurately and consistently, and that communication of the lived experience of disease is strongly represented in the design of the project.

The group proposed that the above framework would enable articulation of the issues and challenges involved with data collection, access and exploitation and the various stakeholders' perspectives on these. It could also serve to highlight examples of best practices, and exemplar case studies.

Aside from using the framework to highlight issues and best practices, it can be a way to tell the story of how collaborative research projects use patient data to realise patient benefit. This would be a very powerful engagement tool to help patients, clinicians, NHS England and policymakers understand how all of the stakeholders use their data to bring new drugs to market.

Developments in Secure Data Environment (SDE) infrastructure

In our previous report, we highlighted the developments in data sharing and how that data can be shared in a secure and effective way through trusted research environments continues to be a hot topic in 2023. The UK has a unique global advantage with the NHS as a source of comprehensive health data for the population. Aligning with the NHS Vision, there is an aspiration to "establish a globally preeminent NHS-centric health data research framework by 2025, one that elevates patient care, fortifies the NHS, and catalyses innovation."

Data is the cornerstone of many TechBio companies and a critical element of this centres on the optimised and secure dissemination of this data via Secure Data Environments (SDEs). Essentially, an SDE is a secure platform that enables researchers to engage with data remotely, circumventing the need to download it directly onto personal devices. While they can retrieve analytical outcomes like result tables or visual representations, the granular

details, especially those of individual patients, remain safeguarded within the confines of the SDE.

A set of subnational SDEs is becoming the default route for accessing NHS data for researchers and SMEs. The government's Data Saves Lives strategy commits to an accreditation scheme and full technical specification for the SDEs, drawing on industry best practices. This includes interoperability, a harmonised accreditation process, and a single point of access. This should both streamline access for data users and provide a higher level of security and transparency for the public on data sharing. There are currently 11 regional SDEs in England, as well as disease specific hubs and commercial data banks. These could offer researchers and TechBio companies a wealth of insight and knowledge, which could then be turned into products and services creating better health outcomes for patients and relieving pressures on the NHS.

The BIA is part of the Life Sciences Council Health Data Industry subgroup which allows our members to influence the development and policies of the SDE implementation strategy and broader data policy.

The BIA's membership of the UK Health Data Research Alliance helps ensure that small and medium enterprises (SMEs) can access and use health research data in an ethical, secure, and efficient manner to accelerate medical breakthroughs. The BIA works with other Alliance members to develop common standards, formats, technologies and tools for the best use of health data and contribute to the development of trustworthy health data research infrastructure.

The BIA is also working closely with the Department of Health and Social Care and its Data for R&D team to facilitate the development and implementation of its SDE strategy. The UK has a unique opportunity to unlock the potential of its health data assets through the SDE network, resulting in better health outcomes for patients and reduced pressure on the NHS.

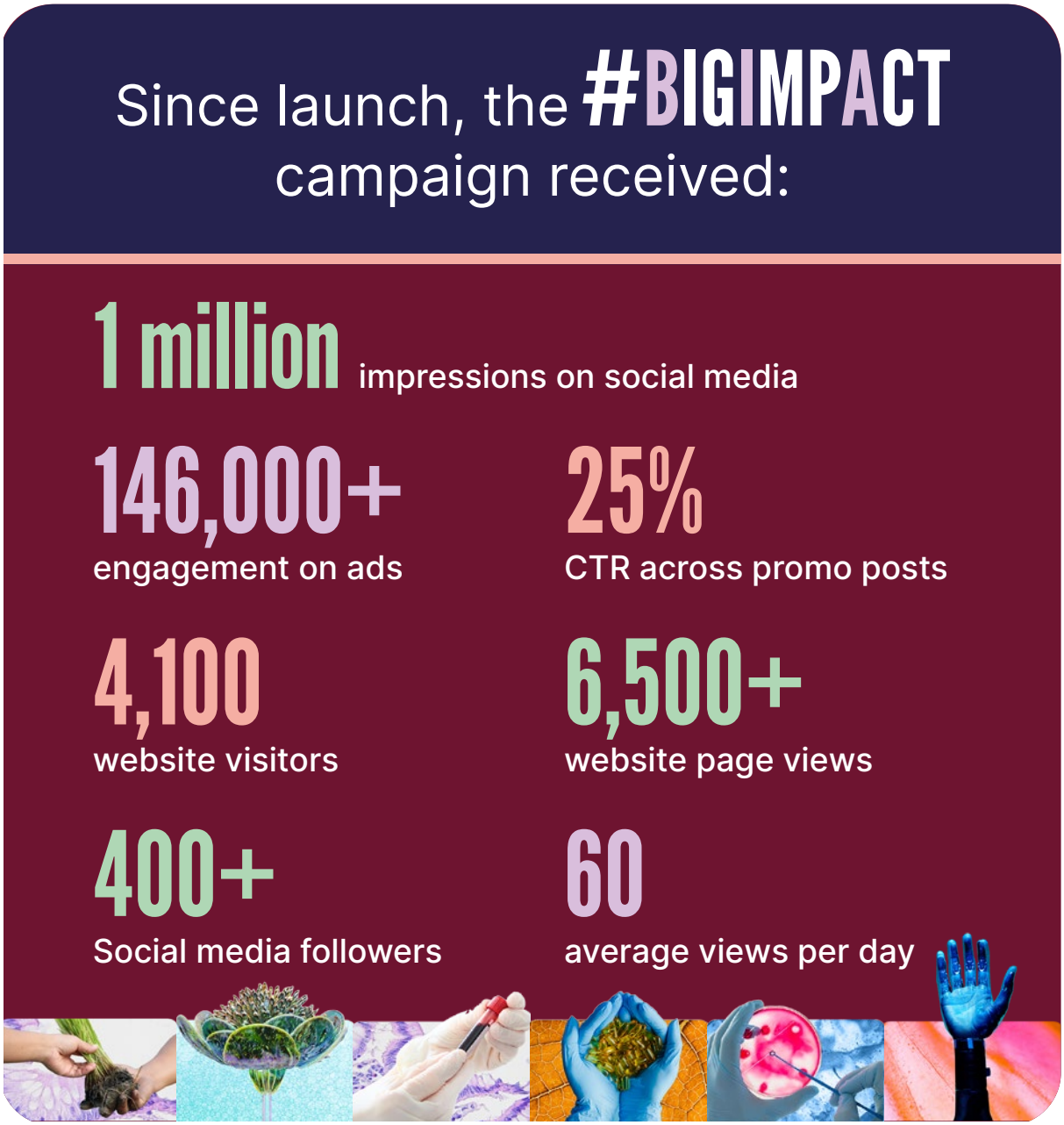
Skills

The BIA's TechBio community has an ever-growing demand for the application of AI/ML and data analytic skills within life sciences. In response, BIA has launched the #BIGIMPACT campaign to address this need.

#BIGIMPACT aims to inspire graduates and seasoned professionals with digital and data-driven skills to pursue a career in the biotech industry. The campaign website bigimpact.org.uk serves as an information hub, for individuals interested in biotech careers. It provides valuable insights into the diverse career opportunities within the sector, including insight into roles such as AI engineers, bioinformaticians and data analysts. The website offers a wealth of resources, including employee spotlights that share firsthand accounts of career journeys, informative white papers, and various other valuable materials. Additionally, it showcases some of the most innovative and impactful companies operating in biotech.

#BIGIMPACT aims to bridge the gap between the tech and biotech sectors by highlighting the opportunities and potential for professionals with AI/ML and data analytics skills to make a meaningful impact in the field of biotechnology.

The campaign is leveraging new social media channels for BIA including Instagram and TikTok. It also seeks collaborations with influencers to reach a wider audience that may not have previously considered applying their skills to the biotech sector. The campaign is gaining traction and attracting both media and policymakers' attention.



Regulation

The BIA has welcomed the Government's commitment to crafting an effective regulatory framework for AI, focusing on key principles such as safety, security, transparency, fairness, accountability, and contestability. BIA strongly supports the idea of empowering industry-specific regulators, like the MHRA, to create nuanced, context-specific regulations, addressing the unique applications of AI in the biotech sector.

BIA recognises the transformative potential of AI in the biotech industry and healthcare, from drug discovery and development to improving patient outcomes, via early-stage

detection and the prevention of disease. The use of AI-based tools has grown rapidly in the past decade to become one of the key drivers for discovering and developing innovative drugs and novel diagnostic tools in the biotech industry.

Moreover, it is suggested that establishing regulatory sandboxes for testing AI systems and encouraging a cyclical approach to regulation will help the UK to keep up with AI's rapid technological evolution. The introduction of additional tools such as ethical guidelines, evaluation frameworks, and data standards will also be beneficial in promoting responsible AI use.

Education for clinicians, researchers, and patients is paramount to mitigate overconfidence in AI tools and ensure their efficacious utilisation. National programs should reinforce technical scrutiny and competitive benchmarking of AI technologies and platforms.

The BIA and the life sciences sector are keen to partner in the development of best practice guidelines for AI applications in health, underlining that community and industry engagement is indispensable for effective regulation. Internationally, there is a strong need for alignment and interoperability with global partners, and we stand ready to contribute to establishing exemplary global AI standards.

By achieving these goals in a collective effort with the government, regulators, and other stakeholders, the UK can enhance its role as a global AI leader, driving growth, prosperity, and public trust in AI applications.

Scaling finance

This report shows the UK leads Europe for TechBio financings but US companies have access to much greater pools of capital to advance their AI and data-driven R&D programmes. This is not a challenge unique to the TechBio sector – it's widely acknowledged that UK life sciences companies are underfunded compared to their US competitors – and BIA is committed to improving access to finance across the ecosystem.

There has been significant progress made since the last TechBio report was published. The Mansion House Compact announced by the UK Chancellor and Lord Mayor of London in July 2023 committed nine pension funds to allocate 5% of their assets under management to unlisted companies by 2030, potentially unlocking £75 billion scaling innovative companies.

The Compact was a watershed moment in BIA's campaign to unlock UK-based institutional capital for investment into UK life science companies. The Compact is complemented by a suite of other policy initiatives including matched-equity funding from the British Business Bank and pension regulatory and reporting rule changes to enable and encourage greater investment from pension funds. The tax environment is also crucial to encouraging investment into scaling TechBio companies and the BIA's influence in the biggest reforms to the UK's R&D tax relief regime since 2000 is ensuring the environment remains a supportive place for companies to start and grow.

We are now working with government, UK life science venture funds and our members to ensure the capital unlocked by all these initiatives is deployed effectively into the sector, including scaling TechBio companies.

Join the BIA TechBio community

BIA's TechBio UK and TechBioX events bring the community together – from start-ups and investors to established TechBio companies, big pharma, policymakers and relevant supporting organisations. If you're a TechBio company looking for your tribe, or a biotech, pharma or investor looking to tap into the potential, come along to our events, join the BIA TechBio LinkedIn Group, and get in touch about becoming a member.

About BIA

The BioIndustry Association (BIA) is the voice of the innovative life sciences and biotech industry, enabling and connecting the UK ecosystem so that businesses can start, grow and deliver world-changing innovation. We are an award-winning trade association representing more than 550+ member companies including:

- Start-ups, biotechnology and innovative life science companies
- Pharmaceutical and technological companies
- Universities, research centres, tech transfer offices, incubators and accelerators
- A wide range of life science service providers: investors, lawyers, IP consultants and IR agencies

Learn more at bioindustry.org

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