Written evidence from bit.bio (ENB0022)

About bit.bio

1. At bit.bio, we have developed our proprietary Cell Identity Coding Platform - capable of producing consistent batches of any human cell at scale and at speed through direct programming of stem cells. Having access to human cells consistently at scale has the potential to transform research, drug discovery and cell therapy, enabling a new generation of medicines. For cell therapies in particular, this has the potential to unblock the manufacturing bottlenecks and reduce cost in a way that would transform access to treatment for a variety of serious conditions, from rare genetic diseases to cancer.

2. The technology addresses two major challenges that have held back the application of induced pluripotent stem cell (iPSC) derived human cells in medical and industrial settings: consistency and scale. Being able to manufacture human cells with consistency and scale opens the door to applications in regenerative medicine, as well as the use of cells in high throughput screening in the context of drug discovery; the generation of reproducible organoids (organ models); and the development of cell standards that help to address the lack of reproducibility that has plagued the life sciences industry.

1. What are the UK's key strengths in the area of engineering biology?

- **Are there any notable research institutes or groups or key projects? Are there innovative companies, start-ups, or spin-outs that you think are of particular promise or significance using engineering biology in the UK today?**

3. Companies (start up and scale up), organisations and institutes are well represented across the disciplines and cycles of engineering biology (known as the Design - Build - Test - Learn (DBTL) cycle). Of particular note are;

    - Basecamp Research, LabGenius (Design)
    - The London BioFoundry, Edinburgh Genome Foundry, Earlham DNA Foundry, University of Liverpool GeneMill, Multus (Design, build, test)

- T-Therapeutics, Expression Edits, bit.bio, Sanger Institute's Programme for large scale 'Generative and synthetic Genomics' (Design, build, test, validate)
- SynbiCITE, established as a synthetic biology accelerator in 2013, serves the national interest as a resource hub for interacting partners from academia, industry and business.
- A notable consortium includes the UKRI funded Mission EngBio Hub - Engineering Biology for Advanced Therapeutics (of which bit.bio is a contributing member).
- TTP and Automata, providing engineering solutions to complex biological problems and automating biology.
- eXmoor Pharma Concepts, providing consulting to the cell and gene therapy space for over 20 years and recently breaking ground on new contract development and manufacturing organisations (CDMO) manufacturing capability.
- Cell and Gene Therapy Catapult and associated consortiums around analytics and manufacturing of cell and gene therapies.
- Roslin CT in Edinburgh, a manufacturing CDMO innovating as the space grows.

4. The sector in the UK is well positioned to develop international partnerships to underpin discovery and development of applications. In March 2024, bit.bio agreed its first project with The Michael J. Fox Foundation[1], the largest non-profit funder of Parkinson's research in the world, to prioritise the discovery and development of a key human cell type for Parkinson's disease. This relationship will provide access to a consistent and scalable source of physiologically relevant human cell models which will help researchers understand and identify the diverse pathways that can cause Parkinson's disease. bit.bio is also working in collaboration with King's College London for the development of multi-cell models of the human brain.

5. We believe there is currently a deficit in the formal coordination between engineering biology organisations focused on health and disease, with opportunity for government and industry to improve in this area.

What is the current economic impact of engineering biology on the UK and what might its potential economic impact be?

6. The breakthrough in cell manufacturing could be compared to the revolution in car manufacturing as pioneered by Henry Ford. Even after the production of the first Model T Ford it would have been difficult, if not

[1] https://www.bit.bio/news/bit.bio-announces-collaboration-with-the-michael-j.-fox-foundation

impossible, to forecast in detail the century of development in the automotive industry and the resulting impact on society and economy which followed. However, informed policy makers of the time would have had a sense of the massive importance of the new industry and the critical national interest in taking a leading position in the application of these new technologies and processes. The comparison here has additional weight, given the need to integrate standard assembly components. For example, bit.bio has created the first technical solution to address the consistency and scale issues in human cell manufacturing, which could have an extraordinary impact.

7. As further detailed in answer to section 2 below, the US has put very deliberate measures and organisations in place for facilitating rapid growth of their engineering biology industries including funding that requires global attention, as they seek to develop a foothold in this next industrial epoch. The engineering biology revolution has commenced in earnest, and disparities between policy and funding will undoubtedly result in further economic, manufacturing, technological and industrial disparities in the very near future (within years). As a consequence, genuine gulfs in global influence within the industry will emerge.

8. Engineering biology borrows its design-build-test-learn (DBTL) principles from classic manufacturing engineering principles. The UK is currently well positioned across these individual principles/disciplines and holds great international esteem in the world of synthetic biology, artificial intelligence and engineering biology, yet struggles to combine one or more within a single company, organisation, or institute. Excellence in bringing pioneering science and world class thought leadership within each core discipline (D, B, T or L) comes at the expense of being able to address the full engineering biology cycle at an industrial scale and pace, due to the expense and infrastructure required and the paucity of mechanisms to support and resource cross-organisational collaboration. These formal support structures are required to consolidate communes of thought leadership in the field across the UK.

9. Due to the rapid development and uptake of synthetic biology, the engineering biology community can design, generate and analyse kilometres of DNA, and perform experiments at a scale and resolution never seen before. However, harnessing the full cycle of engineering biology across the UK is where real industrial change will occur, utilising individual expertise and collaborating across disciplines and organisations. Policies which open these gateways to active and deliberate actions, and the provision of a platform for influencing the

next generation of UK based thought-leadership in science, manufacturing and engineering, are fundamental to unleashing the UKs potential on the global market.

2. What are the key applications for engineering biology?

- **Can you give examples of particularly exciting or interesting applications? In particular, applications which could be taken forward or are being worked on in the UK?**

10. A current example is the medicine Casgevy, gene edited cells authorised by MHRA in 2023 for the treatment of sickle cell disease and transfusion-dependent beta thalassemia. Casgevy impacts patients in the UK living with this disease as well as the UK economy as it is manufactured at RoslinCT in Edinburgh (announced by RoslinCT in 2023).

11. bit.bio's unique cell products are already enabling scientific breakthroughs and applications ranging from the discovery of novel drug targets against Alzheimer's[2,3], the development of biohybrid devices to restore paralysed limb function[4] and outside of human cells, cultured meat. These developments represent true disruptive innovation in stem cell biology, and the first true engineering of human biological systems.

- **Where does engineering biology have the potential to add value over processes that are currently used? What is the nature of this added value (e.g. throughput, sustainability, range of processes that are possible)? Which industries are most likely to be affected?**

12. The engineering of biology holds immense promise in substantially lowering manufacturing costs for goods. bit.bio specialises in genetically programming stem cells to yield pure cell products. This approach streamlines manufacturing complexity, thereby reducing the requirements for input materials and has the potential to dramatically lower the overall cost of goods. Engineered cells enhance manufacturing consistency on a large scale, leading to cost reductions through economies of scale.

- **How does the UK compare to other countries, such as Germany, the US, or China, in terms of investment and policy activity, as well as areas of specialism?**

[2] https://www.embopress.org/doi/full/10.15252/embj.2022113168

[3] https://www.nature.com/articles/s41598-023-31141-6

[4] https://www.science.org/doi/10.1126/sciadv.add8162#

13. bit.bio would highlight the leadership taken by the Federal Government in the United States, as put down in the White House report "Bold Goals for US Biotechnology and the Bioeconomy",[5] which provides 5-year and 20-year specific goals for five areas of the bioeconomy. For example, one area is the advancement of human health with the goal to "increase the manufacturing scale of cell-based therapies… and decrease the manufacturing cost of cell-based therapies 10-fold." For the UK, this emphasises the importance of delivering significant progress and raising ambitions in the first five years of the 10-year Vision for Engineering Biology.

14. The Biden administration has also been responsive for the inauguration of the Advanced Research Projects Agency for Health (ARPA-H), a Federal agency created "to make pivotal investments in breakthrough technologies and broadly applicable platforms, capabilities, resources, and solutions with the potential to transform important areas of medicine and health that cannot readily be accomplished through traditional research or commercial activity".[6]

15. The US framework for the regulation of medicines provides additional resources for developers of innovative medicines such as biologically engineered medicines, including significant educational resources and guidances for development of these medicines, FDA resourcing to provide developers timely access to advice under the Food and Drug Administration's (FDA) drug review process (PDUFA VII), and a variety of programmes to incentivise developers of new medicines that have the potential to fulfil unmet medical need or address manufacturing challenges.

16. Additionally, we acknowledge that Singapore has taken a leading role in creating a supportive environment for the sector, including being the first country to approve the commercial sale of cultured meat.[7]

3. How can Government policy support the development of engineering biology?

17. **Finance:** Compared to other areas of innovation, engineering biology can be especially capital intensive, requiring large amounts of capital. In our case, bit.bio was spun out of the University of Cambridge

[5] https://www.whitehouse.gov/wp-content/uploads/2023/03/Bold-Goals-for-U.S.-Biotechnology-and-Biomanufacturing-Harnessing-Research-and-Development-To-Further-Societal-Goals-FINAL.pdf

[6] https://arpa-h.gov/

[7] https://www.nytimes.com/2020/12/02/business/singapore-lab-meat.html

in 2016 and has raised a total of almost $200 million from Arch Ventures, Foresite Capital, Milky Way, Charles River Laboratories, National Resilience, Tencent, and Puhua Capital, and others. It is notable and obviously disappointing that UK investors have largely been absent in our fundraising to date.

18. We welcome the Mansion House reforms to drive large-scale private investment into high-growth, innovative companies in the UK. It is critical that this effort is driven forward in coming years to unlock capital necessary to unleash the development of the engineering biology companies.

19. **Regulation:** We welcome the ambition to move to a model where regulation is seen as a channel for innovation. Regulators need to be properly resourced, so that they are able to take a forward-looking and proactive approach to developing the best regulatory framework for engineering biology companies. The direction and principles set out in the report by Sir Patrick Vallance and Dame Angela McLean on regulatory reform for life sciences and other highly-innovative technologies could supercharge the UK position as a leading nation for the commercial application of engineering biology.[8] The recommendations to improve and shorten the process in the approval of new medicines and technologies and forge international approval partnerships via the international recognition procedure may be of great benefit for developers planning to commercialise new medicines.

20. Additional support for developers considering conducting clinical trials of innovative medicines in the UK would complement the new procedure for developers considering marking novel medicines. The Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency have emphasised their commitment to supporting development of innovative medicines but do not have the same level of resource as US FDA to provide information and advice to developers of medicines, and guaranteed on-time review of applications for new clinical trial authorisations.

21. Following the UK's departure from the European Union, clarity and consistency must be improved regarding UK regulatory frameworks including the provision of guidance to assist developers in interpreting legislation that frequently has not kept pace with innovation.

[8] https://www.gov.uk/government/publications/pro-innovation-regulation-of-technologies-review-life-sciences

22. The MHRA has advertised its openness to innovation and has supportive programmes (such as the Innovative Licensing and Access Pathway or ILAP), but information surrounding expectations and MHRA resourcing remains a challenge post-Brexit. The US & EU agencies have better information available to sponsors, this despite several EU countries having a reputation for being unfriendly to early development of cell therapies, in contrast to the UK.

23. **Talent and skills:** bit.bio has chosen to headquarter in the United Kingdom due to its world-leading centres of research excellence and pool of skilled researchers, key criteria for the decision of bit.bio to choose Babraham near Cambridge as its global headquarters. Ensuring the UK retains its position as an attractive destination for talent is key in a highly competitive international skills market.

24. **Procurement:** Efficient procurement processes are key to helping companies to innovate and stimulate growth. The public sector is a key stakeholder in the marketplace – a role which other governments often take greater advantage of and use strategically to procure products and services to nurture growth stage companies. This needs to be echoed in the UK to encourage companies to continue to innovate here. One suggestion is to look at the public procurement process in the US, specifically rules requiring, in some cases, buyers to access US providers prior to looking abroad.

25. **Access to laboratory space:** As a Cambridge based company, we note the need for lab space is a salient issue in the Oxford-Cambridge Arc. Growth requires suitable space to grow into, and the planning system and investment required to build these facilities. To this end, growth companies could benefit from Government support to provide guarantees when entering lease arrangements – considering the nature, status of the tenants the risk would be low.

    We welcome recent measures taken by the Government to increase the supply of commercial laboratory space including in the Life Science for Growth Package (May 2023), where the Chancellor committed to increasing laboratory space through pledging to reform planning rules to help scientists.[9] We also note and welcome the focus on Cambridge in the Government's "Case for Cambridge" document, with its focus on making the city the "science capital of Europe".[10]

[9] https://www.gov.uk/government/news/chancellor-reveals-life-sciences-growth-package-to-fire-up-economy
[10] https://www.gov.uk/government/publications/the-case-for-cambridge

26. In addition to laboratory space, there is a good case to provide for more cost-accessible pilot and scale-up facilities, especially bioprocessing, as well as specialist equipment. As bit.bio was progressing towards Good Manufacturing Practice (GMP) manufacturing for clinical cell therapies, it was difficult to find a UK vendor with appropriate facilities. Many existing CDMOs manufacture autologous therapies in small spaces, which are not ideal for bit.bio's larger scale therapies. Encouraging the growth of GMP manufacturing space and incubating manufacturing vendors would also be appreciated.

- **Does the Government's "National Vision for Engineering Biology" set out the right priorities for government to develop the engineering biology field in the UK? The Government has committed to spend £2 billion over the next 10 years on engineering biology. Is this scale of subsidy sufficient to be competitive?**

27. We welcome the Vision and its aims to support our industry and confirm that engineering biology is a key part of the future growth, and health, of the United Kingdom. However, considering the size and potential of the sector, the allocation of £2 billion for the next decade could have been much more ambitious. The next decade represents a critical window to secure the UK's position as a global powerhouse in the commercial development of applications and Government should review additional funding allocations in this context.

4. How can the UK maximise the economic potential of developments in engineering biology?

- **Who is investing in engineering biology in the UK, and what is the scale of the investment activity right now?**

28. As stated above, it is notable and disappointing that UK investors have largely been absent in all the fundraising by bit.bio to date. Investors in the US, Europe and Asia appear to appreciate the value proposition of the UK engineering biology sector more than domestic investors, and are therefore poised to reap its benefits. More must be done by the Government to illustrate the vibrancy, prior successes and future potential of the sector in the UK; the Mansion House reforms are a good start.

- **How well are Innovate UK, British Business Bank and British Infrastructure Bank supporting the commercialisation of engineering biology in the UK?**

29. We would like to see the scope and risk tolerance of British Patient Capital (BPC) extended to include a wider range of companies including those that are in scale-up rather than start-up. If the Government wants to retain UK innovation and talent, then it needs to facilitate funding of companies at all stages of development. BPC is ideally placed to be a significant conduit for channelling appropriate capital to appropriate companies. However, its current risk averse mandate, preference for earlier-stage versus scale-up companies (illustrated by an aversion to considering companies valued at >$150m) and relative lack of resources represents an obvious and currently-missed opportunity.

30. To help growing innovative companies unlock the capital funding they require for continued growth, speed is key. As such, as mentioned above, the creation of the Mansion House Compact is an important statement of intent and leadership between the Government and leading pension companies.

- **What can the Government do to encourage investors to invest in engineering biology and is there a need for investors with more scientific expertise?**

31. There is significant work to be done in terms of raising the level of awareness and understanding of engineering biology in the UK - whether it be across industry, among investors and among generalist policy-makers.

32. For comparison, look at the rise in understanding as regards the integration of Artificial Intelligence (AI) into wider industries over recent years: the 2017 Industrial Strategy[11] identified AI as one of the Grand Challenges where Britain can lead the global technological revolution. Since then, AI has become a focus for Government, with a National AI Strategy (2021)[12] and National AI Strategy – AI Action Plan (2022)[13] to ensure the vision set out in the strategy is being executed. A similar focus is needed on engineering biology following its designation as a critical technology in the Science and Technology Framework, to ensure a greater cross-sector understanding of its wide-ranging applications.

33. To fully leverage the potential of synthetic biology it shouldn't be seen as a stand-alone industry but rather it should act as a positive

[11]https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/664563/industrial-strategy-white-paper-web-ready-version.pdf

[12] https://www.gov.uk/government/publications/national-ai-strategy

[13]https://www.gov.uk/government/publications/national-ai-strategy-ai-action-plan/national-ai-strategy-ai-action-plan

disrupter to others. The Government already facilitates conversations between SMEs and investors, and this can take a similar format.

34. We believe the Government can play a useful and important role in facilitating cross-sector and within-sector conversations between engineering biology companies and companies in other industries to explore the opportunities for innovative applications. In short, Government could facilitate discussions between companies to improve understanding of each other's requirements and explore opportunities for collaboration, including on procurement processes.

35. We must not rely on the Government to overtly seek to 'encourage' investors to the sector, other than pulling levers such as those in the Mansion House compact to increase the potential capital pools. Rather, the Government can do more to illustrate the industry's cross-sector potential and importance to future innovation, which will then help pull investors currently focused on the 'traditional' industries into a new era of synthetic or engineering biology.

6. How should engineering biology be regulated?

- **Who regulates engineering biology in the UK and internationally?**

36. There is not one unified international regulation of engineering biology, although the Cartagena Protocol on Biosafety that seeks to ensure safe use of living modified organisms has been widely adopted, including by the UK. Country and region-specific regulation of genetically modified organisms depends on the context, such as use in medicinal products compared with food. Medicinal products incorporating biological engineering are regulated by the Medicines and Healthcare products Regulatory Agency in the UK.

- **Is the current regulatory framework adequate? Does it strike the right balance between encouraging innovation and ensuring safety? Where should any reforms be enacted?**

37. Our experience is that there is a significant bottleneck in engaging with the MHRA for early scientific advice. Achieving such engagement can be slow, impacting progress and may result in fewer early clinical trials conducted in the UK. The unified Clinical Trial Authorisation (CTA) process with reduced review targets is encouraging, but clear metrics and timeframes for both requests for scientific advice and review of submissions would be valuable to developers due to challenges in planning development in the absence of clear timelines and tremendous expenses incurred during unexpected delays. For instance, the US FDA's

formal meeting and submission review framework with defined timeframes is an invaluable tool for drug developers, providing clear expectations and assisting in sponsors' planning. Additionally, developers can be confident FDA will meet the published targets.

38. The MHRA does have several initiatives to support and encourage development and commercialisation of innovative medicines, including the ILAP programme, the International Recognition Procedure, and participation in Project Orbis, and a commendable risk-based approach to regulation of investigational and marketed medicinal products. Additional guidance to developers of medicines would also be invaluable, especially in light of the complex legislative situation surrounding departure from the European Union.

39. As mentioned in the answer above, we appreciate the ongoing focus of the Government in improving the regulatory environment for high-innovative technologies, in particular the recommendation to focus on streamlined approvals and international partnerships for the MHRA and NICE and the creation of an Engineering Biology Regulatory Network.

40. With regard to therapeutics:
    - The commitment to Cell Therapy in the UK is good with the NHS advanced treatment centres and the work of the Cell and Gene Therapy Catapult. The consortiums organised by the Catapult have made advances in manufacturing and analytics that are key for the industry. The training program fostered in the Catapult has also been instrumental in increasing the available talent in this space. As mentioned above, there is a lack of readily available large-scale cell therapy manufacturing space and the Catapult has made significant efforts to help alleviate this need.
    - We welcome the commitment by the UK to recognise drug approvals elsewhere via the International Recognition Procedure and fast track for approvals here in the future.

41. The regulation needs to remain helpful for cell therapies in relation to synthetic biology. On this point, the Government must be open to the idea of iPSC derived, genetically engineered cells as therapies. There is the potential for the UK to be a world leader as these emerge as a new class of therapies, and the potential of bit.bio to get these treatments to millions of patients through scalable, faster, more cost-effective novel manufacturing.

- **Are regulators sufficiently resourced, in terms of expertise and budgets, to keep up with the pace of change of science?**

42. The Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency have emphasised their commitment to supporting development of innovative medicines but do not have the same level of resource as US FDA to provide information and advice to developers of medicines, and guaranteed on-time review of applications for new clinical trial authorisations.

7. What are the possible barriers and limitations to good and effective use of engineering biology?

- **Does the UK have a sufficient skills base to harness the potential of engineering biology?**

43. A fundamental skill for anyone involved in research within this space as it relates to bit.bio is iPSC – cell reprogramming skills. With respect to functions outside of research e.g. GMP manufacturing, technical operations, project management, having that understanding of how the iPSC forward reprogramming works coupled with that application as it relates to cell therapy is a particularly niche skill set to find.

44. All of our scientists that work within research e.g. molecular biology and functional genomics are required to have iPSC related skill sets. Some of our other functions require a more generalist skill set e.g. molecular biology and cell engineering. We note a shortage of available talent in bioinformatics.

45. Where there are such talent shortages, it is worth noting that competition is global and also against other mature industries, primarily pharma. Machine Learning (ML) talent is particularly hard to incorporate - if you want to train a large language model you need to hire the process power which is incredibly expensive – another infrastructure challenge.

46. Of equal importance are the non-technical skills candidates need to bring to bit.bio and other scale up biotech organisations. For example, strong communication, influencing, project management and collaboration skills are critical to success. The ability to be able to navigate change, deal with ambiguity and operate at a fast pace are key skills for both research and operations in the scale up environment. Investment in training for these softer skills through universities/academic institutions or via Government funded 'access

courses' would be invaluable.

47. It is an evolving process to build a value proposition to attract the individuals we want to work at bit.bio. On this point, one of our strengths is our adoption of a global remuneration policy. We take the US benchmark for salaries and other incentives and as such we are not unduly restricted on where we are able to attract talent from. Despite certain challenges, we have found that our skills pipeline has improved in the 12 months to April 2024. This has largely been down to our ability to sponsor work visas e.g. sponsoring individuals from top UK academic institutions.

48. However, the UK government's recent announcement of changes to immigration rules is a concern. The minimum earning threshold for new Skilled Worker Visas has risen by nearly 50%, from £26,200 to £38,700, making it near impossible for organisations such as bit.bio to hire for certain key roles, especially in the specialist areas in which we operate. The implications for us, and the wider UK science base and STEM sectors, are profound. Overseas workers play a vital role in filling skill gaps and driving innovation. Restrictive immigration policies risk hampering recruitment efforts and slowing down advancements in these critical areas.

49. We would encourage the Government to review these rules for STEM sectors and also to continually review options to increase funding and support for apprenticeships and internships. We also note that for hiring some staff, infrastructure can be an issue e.g. poor public transport links to scientific campuses.

07 May 2024