

## **Written evidence from Constructive Bio (ENB0054)**

### **INTRODUCTION**

Constructive Bio is an engineering biology business deploying breakthrough science from the Medical Research Council Laboratory of Molecular Biology (LMB) at Cambridge University. It is unique in its ability to both rewrite entire genomes and create new to nature biomolecules, incorporating multiple non-canonical amino acids (ncAAs) into a single molecule. Its technology expands the chemistry, and therefore the range, of products that biology can make – in effect programming biology for new applications. Those applications range from creating next-generation therapeutics and building more efficient and sustainable pharmaceutical manufacturing processes to the creation of novel bioplastics and industrial enzymes.

### **What are the UK's key strengths in the area of engineering biology?**

The UK's research and innovation capacity – in both academia and the private sector – has incubated an entrepreneurial ecosystem in which engineering biology startups and companies thrive. State-of-the-art research facilities and institutions across biology, computer science, and chemistry, have also attracted an exceptional talent pool. Taken together, these factors mean the country is ideally positioned to develop and commercialise innovation in synthetic and engineering biology.

Constructive Bio has emerged from this environment as a global leader. Founded in 2021, the company gained an exclusive licence from the Medical Research Council for technology developed by Professor Jason Chin at the LMB. Headquartered in the Cambridge area, Constructive Bio is a platform company based on two core proprietary pillars: whole genome writing and engineered translation. These can be applied to synthesise materials for commercial applications across a range of industries including pharmaceuticals and antibiotics, enhanced agriculture, manufacturing, and materials.

The LMB itself, whose scientists have been awarded 12 Nobel Prizes to date, serves as a catalyst for founding new companies and establishing strategic collaborations for existing ones that are working towards commercialising the capabilities of synthetic biology. The LMB is just one of hundreds of research centres placing the UK, alongside the US, at the forefront of this field.

An increasing number of firms, such as Constructive Bio, are commercialising these discoveries. By 2030 to 2040, the global impact of applications of synthetic biology is expected to hit \$2 to \$4 trillion, and the UK has the potential to spearhead an impactful contribution to these numbers.

## **What are the key applications for engineering biology?**

Our immediate focus for the technology's application is therapeutics. Here, the technology can be used to synthesise functionalised protein and peptide drugs that incorporate exotic chemistries for improved efficacy, and stability and pharmacokinetic properties. New biotherapeutic assets can be produced at scale with unprecedented fidelity and specificity, significantly impacting drug discovery and pharmaceutical manufacturing.

An immediate and timely application for this technology is the development of a more efficient and cost-effective method of manufacturing GLP-1 agonist peptides – the best known of which is the weight management product Semaglutide, sold as Ozempic and Wegovy. Demand for these products vastly outweighs supply and is increasing with new label expansions, but pharmaceutical players are not able to effectively and sustainably produce the drugs at the scale required to meet the growing patient population.

These drugs depend on creating a peptide that includes an amino acid not found in nature, a non-canonical amino acid (ncAA). The ncAA is currently added in a relatively inefficient and wasteful synthetic chemical reaction. Constructive Bio can use engineering biology to express this peptide with the ncAA already in place, significantly streamlining the manufacturing process and reducing the generation of harmful chemical waste.

Engineering biology can also be used to build more effective antibody drug conjugates (ADCs), which deliver drugs to cancer cells – the 'next generation ADCs'. ADCs ensure chemotherapy drugs act on cancer cells without damaging healthy tissue. They bind selectively to target cells and, using a connection called a linker, deliver their drugs directly to the cell.

One of the central challenges in creating ADCs is accurately positioning the right number of drugs on the antibody. Constructive Bio can write the genetic code of the antibody to fine-tune the drug-antibody ratio (DAR) and payload location, and improve the therapeutic index, stability and pharmacokinetics.

The company is also exploring the possibility of engineering ADCs to target a cancer cell with multiple separate drugs through one ADC. This would be a significant technology in cancer treatment where drugs are often used in combination, especially when patients become resistant to certain payloads.

Additional sectors set to be impacted by engineering biology include: plastics and packaging (sustainable and durable biodegradable plastics), electronics (optical films with flexibility and temperature resistance), aerospace materials, agritech and crop care (novel pesticides and herbicides, biologicals that resist genetic transmission), FMCG (speciality peptides, cosmetics bioactives etc.), and

research chemicals (reagents for research labs, biocatalytic enzymes, specialty high-value chemicals and intermediates).

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