Medicines & Healthcare products Regulatory Agency

Executive summary of response to consultation feedback on *Draft guideline on individualised mRNA cancer immunotherapies*

The Medicines and Healthcare products Regulatory Agency (MHRA) has completed a public consultation on its draft guideline on individualised mRNA cancer immunotherapies – a new type of personalised cancer treatment. These technologies use cutting-edge science such as artificial intelligence to design a medicine tailored to each patient's unique tumour profile.

We received responses from across the life sciences community, the NHS, patient groups, academics and international regulators. Feedback recognised the UK's leadership in this area, while calling for greater clarity in some aspects of the guideline.

In response, we will refine the guideline to ensure regulatory expectations are clearly articulated, without hampering innovation. This will facilitate faster access to these promising new therapies, while upholding our standards of safety, quality and efficacy. The final version of the guideline will be published in the coming months, with future updates anticipated as regulatory experience evolves in this rapidly developing field.

- **Scope and Terminology:** In the final guideline we will clarify that the scope is individualised mRNA cancer immunotherapies that use lipid nanoparticle (LNP) delivery systems. We may broaden the scope in the future, as we gain experience with other technologies. A new glossary of terms will ensure correct interpretation of key concepts. The primary focus is licensing requirements, but we will consider guidance on clinical trial requirements.

- **Regulatory Principles**: Most feedback supported our proposal to issue a single marketing authorisation (licence) where a variable component of the immunotherapy is tailored to the patient's unique tumour profile, and to classify these products as advanced therapy medicinal products (ATMPs). Calls were made for a new subclassification of ATMPs to distinguish from genome-modifying gene therapies, and for global alignment. Any proposals to amend the Human Medicines Regulations will be subject to a separate UK Government consultation.

- **Product Design**: Several stakeholders proposed that the regulation of product design should be via the application of Good Manufacturing Practice (GMP), rather than UK Medical Devices Regulations as recommended in the draft guideline. We support this approach, and we will give consideration in the final guideline to regulating product design via the application of GMP where the intended purpose is for product manufacturing.

- **Product Manufacturing:** The feedback was supportive of flexible approaches to batch release, rapid testing, potency assays, and representative stability studies. We will clarify expectations on using representative batches for chemistry, manufacturing and control, and the requirements for traceability between product design, manufacturing, administration and monitoring.

- **Non-clinical Aspects:** Stakeholders sought clarity on applicability of international guidelines, timing of studies, and use of surrogate products. Topics such as tests for immunotoxicity, biodistribution, and HLA matching will be expanded in the final guideline. We will also outline expectations for a staged testing approach.
- **Clinical Aspects:** A broader scope was requested, to include advanced cancer settings and alternative trial designs. In the final guideline we will focus on aspects of trial design arising from the manufacturing time needed for individualised therapies, irrespective of the overall trial design or cancer setting. We agree with stakeholders on the importance of promoting diversity in clinical trials.
- **Post-authorisation:** We will confirm the requirement to conduct a post-authorisation safety study to better understand long-term safety, with registry studies considered acceptable. Patient experience and genomic data in safety monitoring will also be addressed in the final guideline.
- **Patient and Public Information:** Stakeholders stressed the importance of clear, accessible, relevant and culturally appropriate patient information to support decision-making. Information should include how the medicine is made and how long that takes, ingredients, how the medicine is given and how often, what type of cancer it is used for, how the medicine works, side-effects, and the trial evidence to support use. Multiple formats and early communication were recommended. There were calls to ensure any material is co-created with patient experts to ensure appropriateness. These responses will be reflected in the final guideline.