Interacting with UK regulatory agencies to advance cell and gene therapy development

Engagement with UK regulatory agencies

- Cell and gene therapy products are complex and provide unique regulatory challenges when compared to more conventional medicines
- Global regulatory authorities acknowledge that the legislation and guidance cannot keep pace with both the rapid development of the science and the innovative nature of these products
- This has been a key driver for the formation of development tools and procedures that support developers of cell and gene therapies from early to late stage development
- UK Medicines and Healthcare products Regulatory Agency (MHRA) are the forefront of this approach supporting developers in a variety of ways through:
- Innovation Office
- Clinical Trials and Scientific advice
- Early Access to Medicines Scheme (EAMS)
- Innovative Medicines Pathway (coming in 2021)

MHRA Innovation Office

Medicines & Healthcare products Regulatory Agency

- The MHRA Innovation Office (IO) provides a single point of access to expert regulatory information, advice and guidance across the agency
- The IO provides access to expertise and experience from within the agency; the Clinical Practice Research Datalink (CPRD) and the National Institute for Biological Standards and Controls (NIBSC)
- Also provides access to experts from other UK regulatory agencies e.g. Human Tissue Authority (HTA) and Health and Safety Executive (HSE) as part of the (Regulatory Advisory Service for Regenerative Medicine) RASRM
- The IO is more appropriate to developers in the pre-clinical phase as clinical stage development programmes are more likely to require scientific advice
- The advice service is free of charge and intended for innovative medicines e.g. cell and gene therapies, manufacturing processes, etc. and not established technologies
- Broadly equivalent to FDA INTERACT and EMA Innovation Task Force

MHRA Innovation Office

Medicines & Healthcare products Regulatory Agency

- The IO is not intended to be a forum the assessment of data and detailed clinical plans as this is the objective of **scientific advice**, but to gain **regulatory advice** at an early stage to de-risk the programme
- Examples within the scope of regulatory advice may include: viral safety testing plans for a new cell bank, novel manufacturing models for autologous cells, the application of GMP requirements to complex manufacturing processes, application of the risk-based approach to non-clinical studies, etc.
- Go early - the key is to provide concise and informative content, conceptual is fine at an early stage but the more you put in, the more you get out!
- The approach is informal, so provides an easy environment in which to gain valuable regulatory advice for those with minimal experience when approaching regulatory agencies
- Sample case studies are provided by the MHRA:

https://www.gov.uk/government/collections/mhra-innovation-case-studies

Clinical Trials

- The UK is already one of the go-to places in the world for clinical trials involving cell and gene therapies, accounting for 12% of global clinical trials[1]
- MHRA were the first European agency to approve a clinical trial for an allogeneic IPSC-derived cell therapy product (Cynata Therapeutics; 2017)
- More clinical trials initiated for cell and gene products in the UK than any other European country (112 between 2014 and 2019)[2]
- Post-Brexit, clinical trials will be regulated in much the same way in the UK - clinical trial oversight has always been under the jurisdiction of national agencies in Europe
- The standards for the quality, safety and efficacy of medicines will still be equivalent with those set out by the EU framework, OECD mutual recognition of GLP and ICH (International Conference on Harmonisation)

1 Press release: ct.catapult.org.uk/news-media/general-news/press-releaseuk-accounts-over-12-global-cell-andgene-therapy-clinical

2 https://alliancerm.org/wp-content/uploads/2019/10/Trends-in-Clinical-Trials-2019-Final_Digital.pdf

Scientific Advice

- Scientific advice, though not mandated, is recommended in the UK prior to conducting a clinical trial

Objective

To discuss quality (CMC), non-clinical, clinical and paediatric specific considerations, to prospectively de-risk a development programme

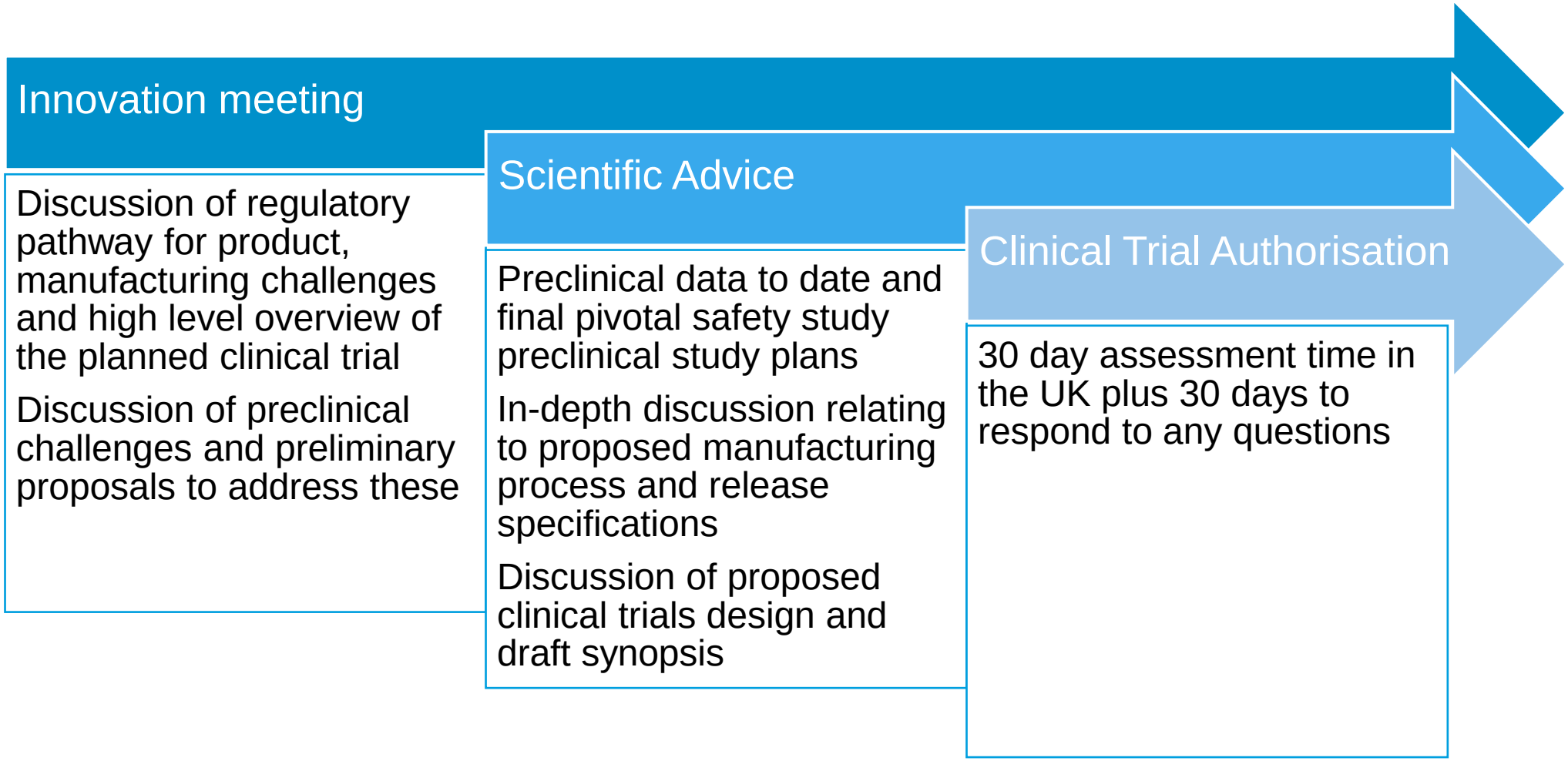
Typical Scope (for a clinical trial)

Presentation of proposed pivotal non-clinical studies, clinical protocol synopsis and manufacturing process and controls

Benefits

- Significantly reduces questions during the assessment phase
- MHRA are known for using pragmatic approaches and scientific principles to guide developers and support their safe transitions from non-clinical to clinical development
- MHRA encourage sponsors to follow up post-advice with any additional clarifications

Typical pre-clinical interactions with UK regulators



Early Access to Medicines Scheme (EAMS)

- UK Early Access to Medicines Scheme aims to ‘give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need’

Eligibility

- Life threatening or seriously debilitating conditions, without adequate treatment options – high unmet need
- Offers significant advantage over and above existing treatment options
- Potential adverse effects likely to be outweighed by benefit
- Able to supply the product to a consistent quality standard (GMP)

Two-step process

- Promising Innovation Medicine (PIM) Designation (based on early clinical data)
- EAMS Scientific Opinion (based on assessment of dossier containing Phase II/III data)

Early Access to Medicines Scheme (EAMS)

Key Benefits

- Prioritised in work programme, particularly through NICE (National Institute for health and Care Excellence)
- Patient access can be brought forward by up to 4 years based on EAMS scientific opinion
- Companies will gain additional knowledge and experiences of these medicines in clinical use.
- Opportunity to generate real world patient data in the NHS, expectation is that medicinal products with a positive scientific opinion could be made available to patients 12-18 months ahead of formal marketing authorisation.
- If an EAMS medicine is subsequently recommended through a technology appraisal, it will then be commissioned by the NHS (National Health Service).

Innovative Licensing Pathway

- The MHRA will launch a new licensing pathway for innovative drugs on 1 January 2021, which shall apply to cell and gene therapy products
- This will include an innovative medicine designation (IMD) and a new target development profile, which will act as a roadmap for the product's development
- This pathway will utilise many of the regulatory flexibilities introduced in response to the COVID-19 pandemic, such as the use of real world evidence, continuous benefit-risk assessment, novel clinical trial design and horizon scanning
- Aim is to enable fast access to novel medicines
- The UK IMD will be broadly analogous to PRIME (EU), Sakigake (Japan) and Regenerative Medicine Advanced Therapy (RMAT) (US) designations
- Key differentiator from PRIME; likely to be combined with market accesses and reimbursement evidence generation and decision making processes

Questions?

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Cell and Gene Therapy Catapult is committed to ensuring high standards of research integrity and research best practice in the activities we carry out. We subscribe to the principles described in the UK concordat to support research integrity.

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