New regulatory routes for cancer treatment in Britain

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*MHRA: views expressed are those of the authors and should not be considered to be formal MHRA policy
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1.Overview

Speed whilst maintaining robust quality, safety and efficacy standards have become an important feature in drug development and patient access. The departure of the United Kingdom (UK) from the European Union (EU) in 2020 resulted in the Medicines and Healthcare products Regulatory Agency (MHRA) becoming a standalone regulator. This independence has provided an opportunity to review the drug development and access pathway. The objective of this paper is to bring the new and current initiatives together in one place for those involved or just interested in the pathway to cancer drug patient access. Under the sponsorship of the Experimental Cancer Medicine Centre (ECMC) Programme Office a multi-stakeholder working group who had previously worked together on a Complex Innovative Design (CID) consensus paper re-formed to compile a summary of the current status of the new regulatory and approvals process.

2. Introduction

From the perspective of drug development, the UK departure from the EU has necessitated a re-evaluation of the clinical trial and drug approval process. It has also meant a need for new routes to replace the European Medicines Agency (EMA) as the main regulator for drug approvals. These post-Brexit routes are highly significant to an oncology community in the midst of its own revolution with new and emerging therapeutic antibodies, checkpoint inhibitors and, latterly, CAR-T therapies replacing the traditional chemotherapy-based treatments. This wave of new agents addressing the needs of an expanding cancer population requires a rapid, responsive and transparent route to licencing and onward to clinic. An overview of the drug development pathway is provided in Figure 1.

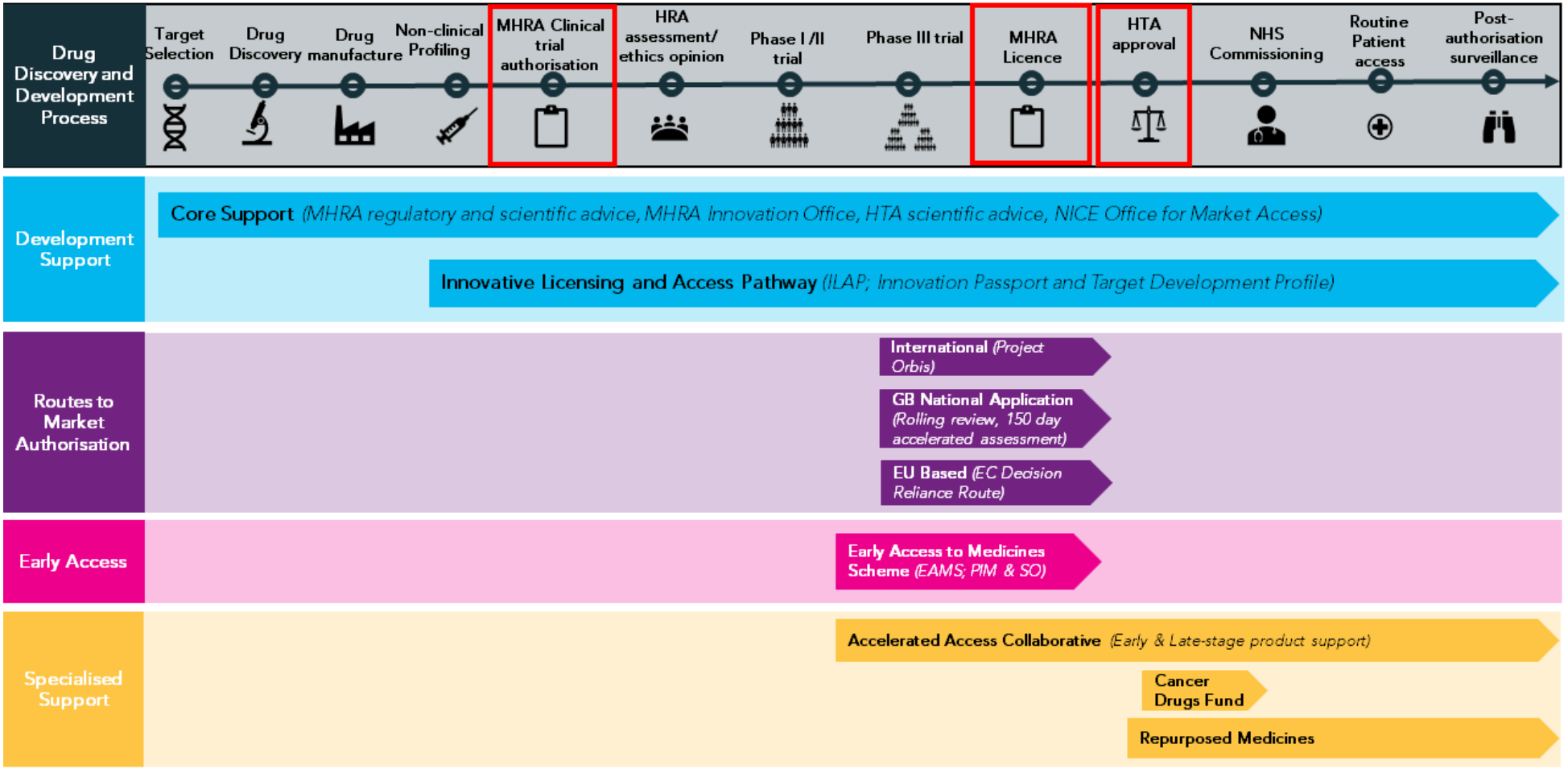

Figure 1. The end-to-end process of oncology drug development, approval and access in Great Britain. The three main approvals milestones are highlighted: initial clinical trial authorisation (CTA) from MHRA, an MHRA marketing licence and HTA (e.g. NICE) approval for prescribing in NHS.

3. Joint advice

MHRA and Health Technology Appraisal (HTA) Advisory Support

Advice from the Medicines Regulator: MHRA offers a variety of services including their innovation office. Early engagement is encouraged and scientific advice can be sought at any point in drug development and can be revisited throughout the development programme. Additional participants to the sponsors are welcomed to the advice meetings such as patient representatives or trial site staff. This may be particularly helpful for programmes involving novel or personalised trial designs.

Advice and support from HTA: NICE offers Scientific Advice and support typically before the onset of phase 3 trials but can be sought at all stages of health technology development. NICE also provides the Office for Market Access (OMA) to life sciences industry partners. Here multiple stakeholders, identified during preparatory discussions, are invited to engage in a structured and extended engagement meeting with the sponsor to discuss issues such as service delivery and commercial options. While sponsors can engage at any stage of product development to gain insights to inform the development of their ongoing market access strategy, OMA engagement offers maximum benefit when undertaken early in the market access and reimbursement process.

Joint Advice: Joint advice is also available from MHRA and NICE. Sponsors will be invited to a face-to-face meeting with NICE, MHRA and a panel of experts at which there is an opportunity to discuss the clinical study design that can satisfy both regulatory and NICE requirements. The outcome is a single report with a joint NICE and MHRA advice summary, exploring health technology assessment, scientific and regulatory issues.

4. Regulatory routes to market

a. Innovative Licensing and Access Pathway (ILAP)

The most significant of these new routes is the Innovative Licensing and Access Pathway (ILAP) launched in January 2021 by National Institute for Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC), and later joined by the All Wales Therapeutics and Toxicology Centre (AWTTC) as a new pathway to support the safe, timely and efficient

licensing and access to innovative medicines. The ILAP partners work with other organisations to provide a single collaborative route for drug development, drug licencing and patient access. Although Brexit was the main stimulus for the ILAP, elements of its design were inspired by other activities including the collaborative and multi-disciplinary RAPID C-19 initiative (Research to Access Pathway for Investigational Drugs for COVID-19) that was assembled to tackle the concurrent COVID pandemic. Rather than being reliant on ad hoc support, the ILAP enables sponsors to obtain end-to-end integrated support from MHRA, relevant HTA bodies and other invited stakeholders. To be eligible to enter ILAP, sponsors must first ensure their IMP programme fulfils the Innovation Passport designation criteria outlined in Table 1. Eligible medicines include, but are not restricted to, novel chemical entities, advanced therapies, medicines for rare diseases, special populations or new indications for repurposed medicines. ILAP is open to both commercial and non-commercial sponsors based within UK or internationally and can support projects in very early stages of development or at mid-development stages.

Table 1: Criteria for obtaining an Innovation Passport

Criteria 1: Details of the condition, patient, or public health area a) The condition is life-threatening or seriously debilitating or b) There is a significant patient or public health need
Criteria 2: The medicinal product fulfils one or more of the following areas: a) Innovative medicine such as an ATMP or new chemical or biological entity or novel drug device combination b) Medicine is being developed in a clinically significant new indication for an approved medicine c) Medicine for rare disease and/or other special populations such as neonates and children, elderly and pregnant women d) Development aligns with objectives for UK public health priorities (Chief Medical Officer, DHSC or Life Sciences Sector Deal)
Criteria 3: Medicinal product has the potential to offer benefits to patients Summary of how patients are likely to benefit, including improved efficacy or safety, contribution to patient care or quality of life, as compared to alternative therapeutic options.

The process of engaging in ILAP is stepwise.

ILAP Innovation Passport: To join ILAP, sponsors are first required to complete an Innovation Passport application online which requires brief information about the IMP and

its target patient population. The passport is allocated to the IMP and a lead indication, previous clinical evidence is not a requirement, and applicants can draw from non-clinical models or other relevant models. Applicants will then be invited to discuss how their IMP fulfils the criteria, usually within 4-6 weeks. The decision to award a passport is made within 4 weeks of this meeting by the ILAP partners.

Target Development Profile: After successfully obtaining an Innovation Passport, sponsors are required to complete a "Target Development Profile" (TDP) submission form providing more detailed information about the development of the IMP, foreseeable goals and challenges as well as the amount of patient engagement required. They are then invited for a meeting with ILAP partners to develop a TDP roadmap. The roadmap is jointly produced with the sponsor; utilising the appropriate tools from the ILAP toolkit to address any issues that may potentially hinder regulatory and access approval. The TDP is designed to be a living document and will include a timeline and milestones as new information is added. This enables upfront descriptions of what is required from sponsors at specific stages along the development programme with the aim of expediting approvals and increasing the likelihood of positive reviews from ILAP partners during the later approval steps.

The ILAP toolkit: Tools within the toolkit are listed on the MHRA website; there are currently eight tools available that can be selected by sponsors to support a "regulation and access ready" development programme. Available tools include continuous benefit-risk assessment integrating real world evidence, access to recruitment populations via the Clinical Practice Research Datalink, increased support for novel trial methodologies, and provision of enhanced patient engagement. Depending on the medicine and the sponsors' position in the development programme, one or more of the tools in the toolkit can be used.

Case study 1: ILAP First Innovation Passport designation: Belzutifan

In February 2021, the first ILAP passport was issued to MerckSharp & Dohme (MSD) as sponsors of the HIF2α inhibitor belzutifan for the treatment of adults with von Hippel-Lindau disease. This is a rare genetic disorder caused by mutations in the VHL tumour suppressor gene (approximately 1 in 33,000 people) and characterised by high incidence of retinal and CNS haemangioblastomas, pheochromocytomas and clear cell renal cell carcinomas. Dr June Raine, CEO of the MHRA said at the time of the designation; 'We're transforming the MHRA to make the regulator an enabler of innovation. I'm very pleased to announce the first Innovation Passport designation demonstrating that this process is well underway. Our Innovative Licensing and Access Pathway is already working to deliver new and innovative treatments to patients through strong and effective partnerships'.

b. GB 150-day assessment for national applications (offered within and outside the ILAP):

The Day 150 procedure aims at accelerating the availability of medicines for patients and includes new active substances and biosimilar products. Under this process, the MHRA will evaluate the application and reach its opinion on approvability within 150 days of submission of a valid application. The MHRA recommend that a pre-submission meeting is requested in order to ensure the process runs smoothly and that the company can receive the full benefit of this review process.

c. GB Rolling review (offered within and outside the ILAP

The rolling review is a new route for Marketing Authorisation applications (MAA, new actives and biosimilars) where sponsors submit increments of their electronic Common Technical Document (eCTD) dossier for pre-assessment by the MHRA rather than as part of a consolidated full dossier submission. The rolling review is intended to streamline the development of novel medicines by offering periodic enhanced regulatory interaction and advice, reducing the risk of failure at the final phase. Following each assessment cycle, a Module Assessment Summary (MAS) will be issued which offers the applicant opportunities to update the module before inclusion in the final phase.

d. EU Based (expected to be outside of ILAP):

European Commission Decision Reliance Procedure: For a period of two years from 1 January 2021, when determining an application for a Great Britain Marketing Authorisations (MA), the MHRA may rely on a decision taken by the European Commission (EC) on the

approval of a new MA in the centralised procedure. This is known as the European Commission Decision Reliance Procedure (ECDRP). Once the EMA Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion, the ECDRP application should be submitted to the MHRA to determine their decision normally no more than 67 days later.

Northern Ireland

After the UK left the EU, the EU and UK signed the Protocol on Northern Ireland (commonly known as the Northern Ireland Protocol) (NIP) which came into force on 1 January 2021. Under the terms of the Northern Ireland Protocol, decisions taken by the European Commission (EC) on the approval of new Marketing Authorisations (MA) in the centralised procedure will continue to be applicable to Northern Ireland.

e. Project Orbis:

Sponsors with an ILAP Innovation Passport who wish to seek concurrent international regulatory review specifically for an oncology indication can now request to participate in Project Orbis. This global regulatory collaboration scheme was established by the US Food & Drug Administration (FDA) in 2019 and from January 2021 the MHRA joined as a Project Orbis Partner (POP) alongside Australia's Therapeutic Goods Administration (TGA), Health Canada (HC), Singapore's Health Sciences Authority (HSA), Switzerland's Swissmedic and Brazil's Agencia Nacional de Vigilancia Sanitaria (ANVISA); all six POPs exist under a shared confidentiality agreement. The FDA will consider applications that would normally qualify for FDA Priority Review, i.e. that would provide a significant improvement in safety or efficacy. By collaborating with regulatory authorities across the world, Project Orbis provides a framework for concurrent submission and review of oncology products among international partners. The first Project Orbis medicine approval in GB was in May 2021 for osimertinib (see Case Study).

Case study 2: Authorisation of Osimertinib under Project Orbis

In May 2021, the first Project Orbis authorisation was obtained by AstraZeneca for osimertinib, an Epidermal Growth Factor Receptor (EGFR) tyrosine kinase inhibitor (TKI) that selectives inhibits EGFR-TKI-sensitising and T790M TKI-resistance mutations. The approval was for the adjuvant treatment of adult patients who had undergone complete surgical resection for early stage (IB-IIIA) non-small cell lung cancer (NSCLC) with EGFR exon 19 deletion or exon 21 (L858R) substitution mutations. Efficacy and safety had been demonstrated in a randomised, double-blind, placebo-controlled study (ADAURA) where the major efficacy outcome measure was disease-free survival (DFS) and where a statistically significant and clinically meaningful reduction in the risk of disease recurrence or death for those treated with osimertinib compared to placebo was observed. The approval was first obtained in USA by FDA in December 2020 but, via the Orbis pathway, marketing authorisation was obtained in GB only 5 months later.

f. The Early Access to Medicines Scheme (EAMS):

The purpose of EAMS, launched in the UK in 2014, is to provide patients that have life threatening or seriously debilitating conditions early access to IMPs (unlicensed or off-label use of medicines) that have not yet had MHRA marketing authorisation but where there is a clear unmet medical need. Effectively, EAMS bridges the gap between an IMP completing positive clinical trials and receiving an MHRA licence, towards the mid to end of its clinical development programme. The MHRA is responsible for the two milestone decisions in the EAMS process: the Promising Innovative Medicine (PIM) designation and the EAMS scientific opinion (SO). Sponsors wishing to be considered for EAMS must first apply for a PIM designation by providing the MHRA with non-clinical and clinical data to demonstrate fulfilment of the EAMS criteria. The next step is the EAMS SO application, providing quality, safety and efficacy data and the risks and benefits of using a medicine before its licence is approved. An SO decision is usually made within 75 days which, if positive, enables physicians to prescribe the medicine funded by the sponsor. EAMS SO end once the MHRA's formal licencing decision has been made although patients on EAMS-approved medicines are allowed to continue treatment until HTA approval (and NHS reimbursement) has been obtained. Since its launch in 2014 there have been over 100 PIM and 50 EAMS SO applications received. Numerous oncology products have been EAMS medicines including pembrolizumab for advanced melanoma (the first agent to obtain SO approval), isatuximab for multiple myeloma and nivolumab for gastric or gastroesophageal junction (GEJ) adenocarcinoma. In June 2020, despite the COVID-19 pandemic, a positive SO was awarded

to Roche's PDL1 inhibitor atezolizumab (Tecentriq) within a new combination regimen for patients with unresectable hepatocellular carcinoma (HCC).

5. Clinical Trials and a single way of working – Combined Review Service

This collaborative approach extends to the combined ways of working initiative by the Health Research Authority (HRA) and MHRA, now called the combined review service[i]. Sponsors are required to submit a complete data package and application including study protocol, patient information and consent documentation for combined review by the MHRA and Research Ethics Committee (REC) . This combined review will be the only review route for clinical trials from the end of 2021 and offers a single application route and co-ordinated review leading to a single UK decision for a trial. Successful review results in both MHRA Clinical Trial Authorisation (CTA) and a positive REC opinion so that the trial can begin in an efficient manner. There is also a fast-track ethics review available if certain eligibility criteria are met, enabling a shorter time between submission and the REC meeting and a faster turnaround of review and correspondence. This may particularly helpful for early phase cancer trials. If using the traditional drug development route, the drug is sequentially progressed through phase I, II and III clinical trials but this route is increasingly being superseded by complex innovative design (CID) trials that merge phases into a single schema or single arm study in rare cancer populations accelerating the evidence required.

6. Access Routes -- Support for drugs in the licencing pathway

a. Accelerated Access Collaborative

In addition to supporting research, access and uptake of medicines, structures have been set up within England to tackle systemic barriers to the adoption and uptake of innovation. The Accelerated Access Collaborative (AAC) was established following the recommendations of the Accelerated Access Review in 2016 as a unique partnership between NHS England, patient groups, industry, and government bodies such as NICE and MHRA to accelerate the development of valuable innovations into the hands of clinicians and patients faster. The AAC is now a dedicated unit within NHS England and NHS Improvement to identify and tackle systemic barriers to the development and adoption of

innovations which can be addressed through partnership working. In the field of oncology, the AAC is working to support the restart and resilience of research within the NHS post-Covid. Additionally, it has an early-stage product support work programme to tackle barriers to access and adoption of histology independent therapies (HITs) and advanced therapeutic medicinal products (ATMPs) see Case Study 3. The AAC is also testing and evaluating artificial intelligence products for oncology as part of the Artificial Intelligence in Health and Care Award. An ATMP roadmap is now available at www.abpi.org.uk/publications/advanced-therapy-medicinal-products-atmps-roadmap-tool

Case Study 3: Uptake of ATMPs by AAC

ATMPs include gene, tissue-engineered and somatic-cell (including CAR-T) therapies. In order to tackle systemic barriers to access and uptake of ATMPs, AAC is working with the Cell and Gene Therapy Catapult to standardise their supply chain, logistics and delivery. They are also ensuring ATMPs are reflected in the NICE Methods Review and are exploring novel reimbursement approaches to support their commissioning. The ABPI has led a multistakeholder workstream to develop a roadmap to guide sponsors through their ATMP journey. This coordinated activity will improve the access and uptake pathway of CAR-T and other oncology products.

b. England's Cancer Drug Fund (CDF):

The CDF was first introduced in 2011 to provide financial resource to fund drug treatments that had not achieved a positive NICE recommendation. From 2016 the CDF was reformed to be delivered as a partnership between NHSE&I and NICE, and become a 'managed access' fund to provide patients in England with access to cancer drugs that had not received a positive recommendation by NICE due to high clinical uncertainty, but where additional data collection could help resolve these uncertainties Cancer drugs funded by the CDF can be made available to NHS patients whilst further data is collected and a NICE re-evaluation is conducted. Practically speaking, the maturation of global clinical evidence development programmes usually provides the necessary data for these second appraisals which have the aim of allowing conditionally approved cancer medicines to obtain full NICE approval with funding provided from NHSE specialised commissioning routine budgets. Additional real-world evidence collected via the Systemic Anti-Cancer Treatments (SACT) database hosted by Public Health England is also harnessed to further supplement the

available evidence and support the evaluation of conditionally approved medicines.

The CDF a remains a critical and vital part of the medicines access architecture. If NICE produces a conditional recommendation, sponsors can work with NHSE&I to formulate a Data Collection Agreement (DCA) and a Commercial Access Agreement (CAA) which taken together are known as a Managed Access Agreement (MAA). It is necessary to wait until a NICE appraisal has progressed and an Appraisal Committee has come to a provisional view about the value of a cancer medicine and where the uncertainties in the evidence base lie before deciding that a managed access agreement with conditional approval is the best way forward. In both scenarios, NICE's Commercial and Managed Access team is on hand to support companies with the necessary dialogues and support. However a CDF recommendation is a requirement prior to approaching the NICE team.

As part of the five-year Voluntary Scheme Agreement on Branded Medicines Pricing and Access (VPAS) negotiated in 2019 between Government and the ABPI on behalf of the pharmaceutical industry in the UK, it was agreed that all new medicines and significant new indications (or "licence extensions") will undergo a NICE appraisal, including all cancer medicines for both common and rarer cancers. This makes the CDF an even more relevant vehicle for ensuring NHS patients can benefit from the latest innovative cancer medicines. The Devolved Administrations of Wales and Scotland do not have equivalent mechanisms for funding of conditionally approved cancer medicines through a cancer drugs fund type

Case Study 4 - Cancer Drug Fund

Histology independent medicines, like larotrectinib, are a new development in the treatment of cancer. These cutting-edge medicines can be used to treat tumours with often rare genetic mutations regardless of where in the body the tumour originated. However, the clinical evidence can sometimes be based on small sample sizes, requiring novel approaches to testing these treatments in clinical trials with translation into models for assessment of potential value to NHS practice.

In May 2020, NICE and NHS England recommended larotrectinib for use on the Cancer Drugs Fund, whilst more data is collected over a number of years on its clinical effectiveness. Following the completion of the data collection period, a further NICE appraisal will be undertaken to decide whether the medicine can be made routinely available on the NHS. In August 2020, NICE and NHS England approved a second histology independent medicine, entrectinib, also for use on the Cancer Drugs Fund.

mechanism. However, both nations do operate a New Medicines Fund which helps to pay for some new medicines. The fund in Scotland is paid for through the national rebates made by the pharmaceutical industry as part of the VPAS Voluntary Scheme. Although separate to the national medicines fund in Scotland, the Scottish Medicines Consortium (SMC) also has the ability to make conditional approval recommendations when a medicine is granted a conditional authorisation by regulatory bodies. This means in practice that the SMC may review again a medicine at the end of the conditional approval period granted by the regulator. In Wales, £16m has been invested in a New Treatment Fund to support access to medicines with a NICE recommendation and to cover the costs of equipment required for treatment administration and clinics for treating or monitoring patients.

7. Repurposing Medicines

The process of Drug Repurposing (also known as Repositioning) describes the re-evaluation of a previously approved medicine for a new indication. Although a strategy of repurposing agents that have already undergone extensive prior regulatory and safety assessments is attractive, the pathway to obtaining a licence for a repurposed medicine has traditionally been challenging. The main constraint has been incentivising industry. For any new drug, pharmaceutical companies utilise the income generated from on-patent sales to fund research and development, licensing and to support the post-authorisation responsibilities of pharmacovigilance, ongoing safety studies and updated labelling and patient information. For a repurposed agent that has completed its original intellectual property life and has become "generic", the lack of novel protection and secure future market position can be a deterrent to pharmaceutical companies and repurposing initiatives tend to therefore be driven by academics or charities. Without a pharma sponsor to support the licensing and post-licensing responsibilities of a repurposed agent, the destination is often "off-label" usage only. This is where a clinician prescribes a drug outside of its original licensed indication (or marketing authorisation) at their own discretion and liability. The lack of trial data of previously approved medicines for new indications can prevent the development of a NICE technology appraisal or a commissioning policy, which sometimes means the prescriber have no clear dosing guidelines or route to refund. NICE however does produce Evidence Summaries for repurposed medicines.

The recent rise in the use of "big data", patient-reported outcomes and enhanced knowledge of cancer biology has heightened interest in repurposing and renewed efforts have been made to make progress. In 2017, the Association of Medical Research Charities

(AMRC) released a series of recommendations around repurposing. Subsequently, NHS England launched the Repurposing Medicines Programme in March 2021, based on the Opportunities to Repurpose Medicines in the NHS in England report. The programme aims to initially support 2- 3 new indications per year to the point of licensing but increasing up to 6 indications/year by year three.

8. Patient and public involvement and engagement

Patient and public involvement (PPI) in cancer research is becoming more prominent to ensure that medicinal and technological innovations for diagnostics, treatment and care correspond with the needs and priorities of cancer patients. Accordingly, organisations involved in cancer drug development and regulation have reflected this shift both in their processes and in their assessment criteria to ensure PPI is embedded at every appropriate stage. In 2019, the MHRA held a public consultation in which patients and members of the public requested more transparency from regulators, inclusion in decision-making and greater responsiveness when concerns were raised. An MHRA Patient Group Consultative Forum was established and PPI strategy was proposed in May 2021. The ILAP partners have initiated pilot projects to integrate the patient voice in the Innovation Passport decision and the TDP activities. The AAC has also developed a Patient and Public Involvement Strategy which is designed to be a blueprint for effective involvement across the joint work of the AAC programmes. Guidance and support is available, ranging from Cancer Research UK's patient involvement toolkit for researchers to ABPI's Working with Patient and Patients Organizations Sourcebook. ECMC's reference guide for patient & public involvement contributors in early phase cancer research contains a comprehensive list of organisations supporting PPI across the UK.

9. Conclusion

The UK's response to the COVID-19 pandemic has highlighted its ability to deliver safe and effective clinical trials in a short timeframe. This has set a precedent for establishing the UK as a world-leader in drug discovery and development. We have described the UK's response to its withdrawal from the European Union which prompted the review of the regulatory pathways, to ensure that all aspects of clinical development and approval are optimised. It is

also clear that appropriate patient and public involvement in cancer drug discovery is becoming ever more important.

The ILAP pathway is a striking example of this modernised and streamlined approach where sponsors, regulators and HTA bodies work in partnership with each other and with embedded PPI to ensure each of the three main approval milestones along the pathway to the clinic are successfully met. Other initiatives such as the MHRA's Rolling review and Day 150 assessment are designed to ensure that medicines both within and outside the ILAP scheme reach patients safety and efficiently. In addition, engagement via the Project Orbis scheme ensures GB works in lockstep with US regulators, enabling regulatory approvals in up to six different nations.

Athough it is too early to see data that supports provides sponsors with a proven and reliable predicted development timeline within or outside the ILAP, there is already evidence that these initiatives are popular amongst commercial and academic sponsors and gives cause for optimism that the UK can be a leading environment for innovative and timely drug discovery and development. It is also clear that appropriate patient and public involvement in cancer drug discovery is becoming ever more important.

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Glossary of terms

AAC	Accelerated Access Collaborative
ABPI	Association of the British Pharmaceutical Industry
AMRC	Association of Medical Research Charities
ANVISA	Agencia Nacional de Vigilancia Sanitaria (Brazil)
AWMSG	All Wales Medicines Strategy Group
CAA	Commercial Access Agreement
CDF	Cancer Drugs Fund

CID	Complex Innovative Design
CAPIG	Clinician and Patient Involvement Group
CHMP	Committee for Medicinal Products for Human Use
CPRD	Clinical Practice Research Datalink
CRUK	Cancer Research UK
CTA	Clinical Trial Authorisation
DCA	Data Collection Agreement
DHSC	Department of Health and Social Care
EAMS	Early Access to Medicine Scheme
EC	European Commission
ECMC	Experimental Cancer Medicine Centre
eCTD	electronic Common Technical Document
EMA	European Medicines Agency
EU	European Union
ECDRP	European Commission Decision Reliance Procedure
FDA	US Food and Drug Administration
HC	Health Canada
HCC	hepatocellular carcinoma
HRA	Health Research Authority
HSA	Health Sciences Authority (Singapore)
HTA	Health Technology Assessment
ICPV	Independent Cancer Patients' Voices
ILAP	Innovative Licensing and Access Pathway
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
MAA	Managed Access Agreement
MAA	Marketing Authorisation Application
MHRA	Medicines and Healthcare products Regulatory Agency
MAS	Module Assessment Summary
MP	Medicinal Product
NHS	National Health Service
NI	Northern Ireland
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NIP	Northern Ireland Protocol
OMA	Office for Market Access
PACE	Patient and Clinician Engagement process
PAPIG	Patient and Public Interest Group
PK	Pharmacokinetics
Patients and service users	Recipients of health care, social care or other services or support provided by or on behalf of health or social care organisations, such as NHS patients and social care service users. Includes people receiving integrated health and social care, e.g. Health and Social Care (HSC) users in Northern Ireland. Excludes children's social care service users in England and Scotland.
PPI	Patient and Public Involvement
PIM	Promising Innovative Medicine
POP	Project Orbis Partner

PROM	Patient Reported Outcome Measure
Public involvement	Working in collaboration with patients, service users or the public in the design, management, conduct or dissemination of research.
RAPID C-19	Research to Access Pathway for Investigational Drugs for COVID-19
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SMC	Scottish Medicine Consortium
SO	Scientific Opinion
Sponsor	The person or body who takes on ultimate responsibility for the initiation, management and financing (or arranging the financing) of a clinical trial.
SACT	Systemic Anti-Cancer Treatments
TDP	Target Development Profile
TGA	Therapeutic Goods Administration (Australia)
UAP	Unfettered Access Procedure
VPAS	Voluntary Scheme Agreement on Branded Medicines Pricing and Access