ROPES & GRAY

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Key Life Sciences Developments to Look Out for in 2023 and Beyond: A perspective from across the pond

MARKET DYNAMICS

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Despite the challenging economic and geopolitical environments, the life sciences sector remains resilient—as it had been at the height of the COVID-19 pandemic. A persistently strong appetite for innovation, irrespective of the economic climate, continues to provide a sustainable level of activity that continues to attract investment. In addition, leading companies have strategic reasons to pursue acquisitions in order to fill the growth gap in the next 5 years in view of, for example, (a) the erosion of exclusivity rights that may present market competition with follow-on products and (b) the necessary growth of the unmet-need market to benefit patients.

- Certain industry players have announced potential acquisition opportunities in 2023 which focus primarily on immunology and oncology, but other therapeutic areas such as neurology, cardiovascular diseases, orthopaedics and vaccinology could also be in play. Products developed for rare diseases are of particular interest. Orthopaedics and cardiology remain key areas for growth for the medical technology sector. The normal market sweet spot for deals in the range of US$ 5 to 15 billion will likely continue, but some expect that more deals in the region of US$ 30 billion plus in the latter part of 2023. Promising science and technology with significant differentiating features will remain the key driver for strategic transactions. Contract firms specialising in research and development ("**R&D**"), manufacture, and distribution activities are becoming attractive targets for investment.

- Thanks to the continued momentum in advancing the genomic revolution and in the advent of next-generation sequencing that has made it possible to cheaply and reliably sequence entire genomes, transcriptomes, proteomes and metabolomes, there is a continuing interest in the development of the next generation of products based on advanced therapies and targeted therapies. A considerable number of these innovative products are approved in the United States, the European Union and other key international markets.

- Combination approaches are increasingly being developed and adopted to maximise therapeutic effects and to improve patient outcomes.

- Interest in R&D of nucleotide-based technologies, particularly ribonucleic acid therapeutics, to repair gene defects or modulate gene expression, has intensified.

- Equally significant advances are observed in the medical technology sector such as mechanobiology to enable high-precision measurements of a broad range of soft biological tissues; MRI-guided radiotherapy to enhance precise targeting capabilities and reduce toxicities; and wearable skin patches to monitor specific markers in blood chemistry.

- New technological approaches are being adopted by researchers to improve efficiency in R&D, including greater use of artificial intelligence ("**AI**"), machine learning and robotics being applied at various stages of the product life cycle.

- Digital transformation is being pursued within the health care setting with the aim of improving patient care and management.

- Digitalisation coupled, with other technological platforms, is revolutionising the way big data are collected, collated, synthesised and managed which may be helpful to inform regulatory decision-making concerning product approval and market access; specifically, researchers and regulators are embracing alternative methodological approaches to generating big data in a real-world setting. Real-world data bridge the gap between clinical research conducted in an artificially homogeneous setting and practice in health care by allowing manufacturers to study how patients actually use and respond to an approved new product.

REGULATORY AND MARKET ACCESS ENVIRONMENT

In view of the ongoing R&D efforts, unsurprisingly, regulators and payers deciding the fate of market access of new therapies will need to respond to the continuing scientific endeavours and medical advances to ensure that the regulatory and market access systems remain relevant to foster research into new technologies and treatments. The evolving regulatory environment will have a significant bearing on timely access to effective treatment for patients. With these considerations in mind, this outlook identifies a number of key regulatory developments to look out for in 2023 and beyond. Although the focus of this update is placed on the European Union and the United Kingdom, these considerations would similarly resonate in other geographical regions in view of increasingly globalised cooperation amongst authorities via various harmonisation and coalition initiatives.

EVOLVING PHARMACEUTICAL LEGISLATION AND REGULATORY POLICY

- In order to embrace new therapeutic approaches to benefit public health and patients, there is a greater recognition for regulatory innovation to ensure agility of the regulatory framework to support access to novel health technologies whilst continuing to protect public health and patient safety. Indeed, the pandemic reinforced the need for regulatory agility to support timely access to necessary health care products without compromising safety, quality and efficacy, and this position resonates across the globe.

  Reform of EU pharmaceutical law

  - Following the European Commission's Pharmaceutical Strategy for Europe, plans are in place to reform the European Union's general pharmaceutical legislation. This legislation, which was last reviewed in the early 2000s, has not kept pace with technological advances. Its deficiencies were laid bare by the pressures of the COVID-19 pandemic. The current plan is for the proposed revision to be published in the first quarter of 2023. The proposal is expected to address issues concerning improved access to medicines, revision of the wholesale distribution licensing system and novel incentives for the development of antimicrobials addressing antimicrobial resistance. In addition, the regulatory exclusivity rules will likely be reconsidered to balance incentivising innovation on one hand and market competition on the other.

  Clinical development and management of data sources and health data

  - In order to accelerate clinical trials, many key global regions or countries have developed regulatory policies to facilitate decentralised clinical trials ("**DCTs**"). Through greater use of digitalisation, including telemedicine and health mobile applications to enable remote patient monitoring, DCTs aim to make it easier for eligible subjects to participate in clinical trials by reducing the need to travel to trial sites, thus widening the demographic of participants and reducing dropout rates. In addition, as part of the broader agenda relating to good clinical practice modernisation, regulatory authorities recognise the new opportunities for novel and innovative clinical trial designs and methodologies. It is envisaged that there will be regulatory policy development on complex trial designs, such as umbrella trials and basket trials, or master protocols, including advanced biostatistical and data analytics. Recruitment of patients

may also change with the use of new technologies to identify eligible study participants and new ways to capture data during clinical trials.

- In response to increasing use of big data derived from various sources to support regulatory and market access decision-making, greater scrutiny will be placed on the quality of the data sources to determine whether the data can be relied upon to inform regulatory decision-making. Additionally, in May 2022, the European Commission proposed a regulation which would create a health data ecosystem known as the European Health Data Space ("**EHDS**"). If adopted, the EHDS would fully harmonise electronic patient records throughout the European Union and facilitate the portability of patient records across member state borders. This colossal database could be accessed for the purpose of providing health care as well as secondary purposes such as policymaking and research by industry. Each use would be underpinned by clear rules, common standards and practices, infrastructure, governance, security, safety and privacy. The Commission has ambitiously communicated that its "target is for the Health Data Space to start functioning by 2025". However, significant challenges will need to be overcome before the launch of the EHDS. Currently, the proposal is in draft form awaiting the Committee's decision.

- Conduct of clinical trials in the European Union has transitioned to the new framework under Regulation (EU) 536/2014, the EU Clinical Trials Regulation ("**CTR**"), and, on 31 January 2022, the Clinical Trials Information System ("**CTIS**") went live. After 31 January 2023, sponsors must submit initial clinical trial authorisation applications via CTIS. By 31 January 2025, all ongoing trials approved under the old regime will be governed by the CTR and will have to be transitioned to CTIS. In the United Kingdom, the Medicines and Healthcare products Regulatory Agency ("**MHRA**") ran a public consultation in Q1 2022 on proposals aimed at updating the regulatory framework applicable to clinical trials in the United Kingdom. The results of that consultation are in the process of being analysed. If the proposals are taken forward, they would be subject to parliamentary scrutiny prior to becoming law.

<u>Digitalisation: Artificial intelligence and related technologies</u>

- As part of the European Union's AI Strategy, the Commission has proposed a first-of-its-kind regulatory framework on AI comprising a Regulation laying down harmonised rules on AI (the "**AI Act**") and a Directive on its associated non-contractual civil liability profile (the "**AI Liability Directive**"). In its current draft, the AI Act distinguishes between uses of AI that create unacceptable risk, high risk and low/minimal risk. If adopted, high-risk AI systems will need to meet comprehensive requirements, such as those related to data governance, recordkeeping, transparency, accuracy and security. Low/minimal-risk uses of AI will need to abide by transparency obligations. The AI Liability Directive seeks to give businesses legal certainty on their exposure to liability ,whilst simultaneously ensuring that the legal framework is fit for the increasingly digitised economy. The new regime lays down uniform rules for access to evidence and alleviation of the burden of proof in relation to damages caused by AI systems, thus establishing broader protection for an injured party to seek redress. It also introduces a presumption of causality against the developer, provider or user. Given the novelty of these proposals, their impact on businesses and their cross-sector application, it is anticipated that the progression of the AI Act and the AI Liability Directive through the legislative process over the course of 2023 will be protracted.

- In contrast to the European Union, the United Kingdom is currently pursuing a decentralised approach to the regulation of AI. Industry regulators, such as the MHRA, are charged with developing regulatory regimes specific to the industries they regulate. The MHRA's Software and AI as a Medical Device Roadmap details 11 work packages covering items such as regulatory guidance, secondary legislation, and pre- and post-market obligations. Certain of these deliverables will be covered by the new medical device legislation which is currently being prepared in the United Kingdom.

Quality assessment

- Complex medicines currently being developed will require either new approaches or the adaptation of existing approaches to the evaluation of product quality through catalysing the integration of science and technology in medicines development and control to facilitate implementation of novel manufacturing technologies based on physical and material science. Modernisation of good manufacturing practice would need to be critically considered to fully embrace emerging technology in the evaluation of product quality.

EU regulation of medical devices

- Practical implementation of the new regulatory framework provided by Regulation (EU) 2017/745 on medical devices (the "**EU MDR**") and Regulation (EU) 2017/746 on in vitro diagnostic medical devices ("**IVDR**") remains controversial. The new regulatory regimes overhaul the pre-existing framework under the Directives governing general medical devices, active implantable medical devices and in vitro diagnostic medical devices (the "**EU Device Directives**"). However, the deadlines set out in the transitional arrangements of the EU MDR are now recognised by the EU legislature in the European Health Council and the European Parliament to be unrealistic, with the potential to cause significant harm to health systems and patient care in the EU Member States. On 6 January 2023, the European Commission issued a proposal which, if adopted, would significantly extend the deadlines of transitional provisions. For a detailed analysis of these proposed deadlines, please refer to our earlier alert.

- The existing medical device legislation in the United Kingdom, the Medical Devices Regulations 2002 (the "**UK MDR**") was passed in order to give effect to the EU Device Directives, which preceded the EU MDR and which were originally drafted in the 1990s. Since the EU Device Directives and UK MDR took effect, the pace of technological advancement and the intensity of innovation in the medical technology sector has been significant. As mentioned above, this led to regulatory reform at the EU level in the form of the EU MDR and IVDR. In practice, this means that the regulatory framework applicable in the United Kingdom is based on the outdated EU Device Directives. In order to correct this, from September to November 2021, the MHRA launched a public consultation on proposals for reform (see our earlier alert for a discussion of the proposals), the government response to which was published on 26 June 2022 (see our earlier alert for a summary of the key points). Originally, the new framework was scheduled to coincide with the last date that EU-approved devices could be placed on the UK market. However, it has recently been decided that this will be delayed by 12 months, with the new regulations now planned to enter into force in July 2024.

Continued international cooperation

- There is an increasing need to engage external stakeholders, such as patient organisations and health care professions, to assist in assessing the clinical relevance of outcome measurements. The regulatory scrutiny over the probity of such engagements will not be diminished.

- In an increasingly globalised market where diseases have no geographical borders, increased international cooperation and partnership amongst regulatory and enforcement authorities will continue to avoid duplication of efforts and to ensure alignment of regulatory approaches to promote the best use of limited resources.

Pricing and market access

- Controversy surrounding pricing and reimbursement in determing market access to innovative medicines and technologies will continue to attract a great deal of debate. Significant pricing controls, including significant clawback payments, to contain health care costs have been increasingly applied in many European countries in order to respond to acute pressure on budgets. New national laws and/or policies are being considered or passed with the effect of tightening drug pricing and reimbursement rules. Some have already called for sustainable pricing policies to incentivise investment in innovations. In the United States, aside from the Inflation Reduction Act, which introduced price negotiation on some drugs, the Institute for Clinical and Economic Review reported that whilst many key elements of fair access were not able to be assessed, there is high concordance amongst major payer coverage policies in respect of fair access criteria related to cost-sharing, clinical eligibility, step therapy and provider restrictions.

BREXIT CONSEQUENCES ON REGULATION OF MEDICINES AND MEDICAL TECHNOLOGY

- Whilst the United Kingdom is a relatively small market, its standing in global life sciences regulation remains influential. That said, the local regulatory and market access environment may need to be adapted in order to achieve the Government's stated ambition of making the United Kingdom an attractive country to conduct clinical development and to launch new products. The local market access environment must be sufficiently flexible for new products to be adopted for use in the National Health System. The success of the newly created flagship initiative, the Innovative Licensing and Access Pathway, created to accelerate the time to market, is critical to the future of the UK life sciences ecosystem.

- In addition, Brexit continues to reverberate within London and Brussels. Apart from the current debate on the Northern Ireland Protocol, the most impactful legislative challenges would be the status of retained EU law in the United Kingdom. The UK Government's stated policy is to capitalise on Brexit so that the rules and regulations best serve the UK national interest. In the context of the life sciences sector, the United Kingdom's pharmaceutical regulatory regime is firmly rooted in EU law as well as applicable EU-derived soft law guidance. However, on 22 September 2022, the United Kingdom's Department for Business, Energy & Industry Strategy published the Retained EU Law (Revocation and Reform) Bill 2022 (the "**Bill**"). The Bill seeks to provide a basis for amending or revoking over 2,400 well-established retained EU laws ("**REUL**") that operate across 21 sectors of the UK economy, including the life sciences sector, by 31 December 2023. The Bill, if passed in its current form, will mean that the majority of REUL must either be reformed, adopted, revoked or left to expire on 1 January 2024, which would have significant ramifications for the life sciences industry and others. See our previous alert here.