TRENDSPOTTING 2022: ON THE PULSE OF LIFE SCIENCES

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Introduction

The global life sciences industry is evolving at an extraordinary rate. Scientists are rapidly gaining insights into fundamental biologic processes and novel cures. Cutting-edge developments and basic science are transforming medicines, medical devices, and diagnostic tools. Industry participants are collaborating to bring products to market in novel ways, and sophisticated investors are fueling this remarkable set of developments. Healthcare products are being delivered to patients worldwide through complex channels, and being reimbursed through an array of payors. As a result, the industry today is vastly different from what it was even five years ago, and it will be vastly different five years from now.

The pace of technological development is unprecedented and offers the potential to revolutionize treatment for some of today's most devastating diseases and conditions. However, these changes give rise to a host of complex legal and regulatory issues impacting both life sciences companies and their financial backers. Governments are exploring ways of regulating new products to ensure that they are safe, effective, affordable, and accessible, but the nature of some of these products requires innovative licensing and collaboration agreements to unlock their potential. The novel form of many emerging products is also becoming a greenfield for IP disputes.

Here, Sidley's Global Life Sciences group looks at 12 forces driving the life sciences legal and regulatory landscape in 2022, and provides practical tips on a range of topics for life sciences companies and investors seeking to navigate through, and capitalize on, this complex environment.

For ease of viewing, please use the jump links in the pages below or the bookmarks in the left-hand toolbar to navigate to specific areas of interest.

KEY TRENDS:

Global Drug Pricing

This year, the U.S. Congress will identify policy alternatives that impact prescription drugs, while EU and member states will remain focused on driving down drug prices. In the UK, drug pricing procedures are expected to align with the pricing of companion digital tools.

Digital Health and AI

Wearables and mHealth will increasingly be used to collect real-world data for use as real-world evidence in regulatory decisions. New regulatory frameworks that cover AI and digital health are on the horizon in the U.S., China, and Europe.

FDA New Intended Use Regulation

Drug and medical device manufacturers in the U.S. may have increased potential exposure in off-label promotion cases, as a result of the FDA's new "intended use" rule. Manufacturers' safe-harbored communications about new uses of lawfully marketed products may also be affected.

Current Good Manufacturing Practice Compliance

Life sciences companies can expect a more robust inspectional effort from regulators worldwide. Regulatory authorities are likely to be more vigilant in their inspections. Manufacturing sites situated in a different country from corporate headquarters are likely to be particularly vulnerable.

Privacy

In the U.S., we will see an increase in privacy and cybersecurity-related enforcement actions. In Europe, more guidance will be published on areas of digital health such as AI. In China, new laws and forthcoming guidance will have a significant impact on how life sciences companies process data.

Licensing

The accelerating pace of development of combination therapies complicates the structuring of licensing agreements. New regulations

around pricing and market access also will make partnering increasingly complex, even for early-stage assets.

IPOs

U.S. and Hong Kong investors are taking a more cautious approach toward investing in pharma and biotech in 2022 as public company performance has trailed broader markets in 2021. In China, investment will trend toward tech, including life sciences. We will increasingly see Chinese-founded life sciences startups seeking IPOs in China, Hong Kong, and the U.S.

U.S. Special Purpose Acquisition Companies

The number of life sciences SPACs is expected to continue to increase in 2022, despite increased scrutiny by the SEC.

Antitrust and Competition

Enforcement actions and investigations are likely to accelerate in relation to M&A and pricing and distribution. We expect to see more "excessive pricing" cases brought in the life sciences sector. International cooperation on life sciences deals between national antitrust agencies will likely increase.

Private Equity Investor Risks

In the U.S., both the government and whistleblowers are pursuing PE investors in FCA cases based on alleged violations of healthcare fraud and abuse laws. Both majority and minority investors are exposed to this FCA risk.

IP Litigation

There is likely to be a move away from patent litigation over mechanical devices toward medtech innovations that rely heavily on software implementation. We anticipate more litigation around nonpracticing entities and more litigation involving biologics.

Arbitration

We expect to see an increase in disputes over earn-out clauses in M&A transactions and third-party funding of significant claims in arbitration. It is also likely that there will be a rise in investor-state claims alleging breach of international investment protection agreements.

Global Drug Pricing: New reporting burdens may impact future product development in the U.S., UK, and EU

DRUG PRICING TRENDS:

U.S.

– In the U.S., Congress will remain focused in 2022 on identifying policy alternatives that can have a dramatic impact on reimbursement, pricing, and innovation of prescription drugs.

– In particular, we expect Congress to continue to focus on policy alternatives set forth in H.R. 5376, the Build Back Better Act.

EU

– The EU and member states have been focused on driving down drug prices since 2016, and that focus has sharpened since the pandemic.

– 2022 will provide unique challenges and opportunities for industry to preserve and improve EU pharmaceutical law.

UK

– Drug pricing procedures are expected to become aligned with the pricing of companion digital tools.

– More pressure is likely to be put on life sciences companies to disclose costs as a justification for pricing.

U.S.

We anticipate that the U.S. Congress will remain focused on policies that could have a significant impact on the reimbursement and pricing of prescription drugs — and ultimately on innovation in the industry, if passed and implemented. These include the Build Back Better Act's policies relating to negotiation for some medicines covered under Medicare, inflation rebates in Medicare, and capping out-of-pocket spending in Medicare. Even if not passed under the Build Back Better Act (which itself may not pass), be prepared for continued focus on these policy alternatives in other legislative vehicles.

In 2022, life sciences companies will also need to prepare for the Refund Act, which introduces new requirements on manufacturers of physician-administered products to conduct enhanced monitoring and input procedures beginning January 1, 2023. This unprecedented development will require pharmaceutical manufacturers to provide quarterly refunds to Medicare for unused portions of certain physician-administered drugs. The industry will also need to prepare for the implementation of the Medicaid program's value-based purchasing regulatory provisions in July 2022. Operational guidance on the latter is expected soon.

We also expect the trend for litigation and regulatory actions against drug pricing developments that unfolded under the previous U.S. administration to continue in 2022 under the Biden administration. In particular, manufacturers of outpatient prescription drugs should monitor litigation, administrative, and regulatory developments related to the 340B Drug Pricing Program and the Medicaid Drug Rebate Program. In addition, in connection with the Medicaid program, the forthcoming implementation of new regulatory burdens associated with line extensions and the expanded definition of "States" to include the U.S. territories may significantly impact the net pricing of drugs under the Medicaid program. This is in addition to the already significant increase in the regulatory burden manufacturers are expected to face in calculating and reporting detailed pricing information to the Medicaid program.

EU

In the final quarter of 2022, the European Commission is expected to propose new pharmaceutical legislation pursuant to its "Pharmaceutical Strategy for Europe." This new legislation is likely to affect the fundamentals of current EU pharmaceutical law. It may restrict the scope and duration of IP and regulatory rights (e.g., regulatory data protection, rewards and incentives for pediatric and orphan medicinal products, and patent term restoration rules), in particular in situations where companies do not disclose R&D costs and/or do not launch their products in most or all EU member states.

Separately, the European Commission will start setting up the mechanisms for the roll-out of the recently adopted HTA Regulation (2021/2282), which provides for mandatory joint clinical health technology assessment of new centrally authorized drugs and selected medical devices as of 2025. In the meantime, the Commission will continue to support HTA cooperation between member states.

The new pharmaceutical rules and HTA cooperation, coupled with the ongoing budget pressures caused by the pandemic, will accelerate the push by the EU and individual member states to drive down drug prices. Throughout 2022, we are likely to see political discussions about drug pricing, and by the end of the year, we are likely to have more clarity on the extent to which value-based pricing will be complemented or replaced by a cost-based, R&D expenditure-focused approach to pricing and reimbursement.

Whether a value-based pricing approach prevails will depend upon whether the EU institutions, together with national pricing, reimbursement, and antitrust authorities, accept that biopharmaceutical product development is not simply a question of R&D expenditure. If the R&D expenditure-focused approach to pricing does gain momentum during 2022, this is likely to have the greatest impact on smaller companies that lack a large portfolio through which to spread development risks.

2022 is therefore likely to present great challenges and opportunities for the life sciences industry to preserve and improve EU

pharmaceutical laws. Life sciences companies should participate fully by making their views heard, either directly or via trade associations.

At the EU member state level, litigation will continue in antitrust cases regarding alleged "excessive pricing" and the replacement of authorized drugs by "replacement pharmacy compounding."

UK

Post-Brexit, the UK government has been moving to expand the country's platform as a key location from which to develop and invest in life sciences. In 2022, product development for smaller life sciences companies is likely to particularly benefit from stronger support from the key authorities in the UK. We also anticipate that innovative drugs will experience accelerated access to the UK market. Similar pathways that are also being explored for digital health technologies may materialize.

A range of new legislation has been introduced in the UK to facilitate life sciences. This is in part directed toward enabling faster access to the market for innovative digital technologies. UK health authority NICE — similar to the health authorities in other European countries — has updated its evidence standards framework for digital health technologies and has established a new Office for Digital Health. The UK government has also put aside a particular fund to support e-health technologies.

In 2022, more guidelines and procedures are expected to become available for digital health and AI technologies in the UK. It is not clear how these technologies will be priced and whether they will be aligned with the pricing of the associated drugs. Under the new proposed UK Medical Devices Regulation, there will be a new legal framework for software and AI devices that may be regulated as medical devices.

DRUG PRICING TIPS:

U.S.

– Life sciences companies should continue to assess their advocacy, regulatory, and litigation options with respect to aggressive drug pricing policy alternatives in 2022.

– Life sciences companies and their owners and investors should carefully consider the drug pricing legislative and regulatory proposals at the federal and state levels when evaluating coverage and reimbursement options for their products.

EU

– Life sciences companies should follow regulatory discussions closely and take on likely outcomes in clinical product development and regulatory decisions to ensure that products qualify for rewards and incentives.

– Companies should expect to meet an increased burden of proof to obtain pricing and reimbursement.

UK

– Life sciences companies should set up a product-specific "task force" with experts in various disciplines. Market access and pricing need to be considered from the outset, including when planning and designing clinical trials.

– Life sciences companies should prepare their market access at an early stage to ensure that they will be able to satisfy NICE's cost-effectiveness criteria.

Contacts

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Digital Health and Artificial Intelligence (AI): Rapid development of new technologies and regulatory frameworks will transform the sector

DIGITAL HEALTH AND AI TRENDS:

Wearables and mobile health will increasingly be used to collect real-world data (RWD) for potential use as real-world evidence (RWE) in regulatory decisions.

New AI and digital health regulatory frameworks are on the horizon in the U.S., China, and Europe.

Medical software to support physician decision-making and medical robotics will continue to evolve.

Digital diagnostics and digital therapeutic medical devices have emerged as an exciting opportunity to innovate in the provision of healthcare, but require careful planning as to coverage and payment.

Enhanced use of AI raises new questions about tort liability and risk mitigation.

Much of the rapid change that the life sciences industry is currently experiencing is technology driven. The growth of digital health is likely to be a defining feature of the decade for the industry. Fast technological advancements mean that AI technologies will reach mainstream adoption in the next five years. The International Data Corporation has estimated that worldwide spending on AI across all industries will increase from the US$50.1 billion spent in 2020, to more than US$110 billion by 2024.

The impact of digital health and AI will be much wider than new products — such as wearables and diagnostics — and new processes — such as decentralized clinical trials. We anticipate that, with the advent of cloud-based, off-the-shelf AI tools, AI technologies will become more widely accessible and affordable. New types of life sciences companies will arise within the industry, and will face a diverse and novel legal and regulatory landscape in relation to the use and commercialization of digital technologies.

Developments will be spurred, in part, because life sciences companies and regulators are increasingly using RWD — data generated by patients and doctors outside of clinical trials — as RWE to support a range of product development and regulatory decisions.

Wearables and mobile health (mHealth) technologies will enable the increased collection and evaluation of digital biomarkers, measurable indicators of a biological state or condition, that provide valuable data for the application of AI systems. Edge AI applications, which run AI algorithms locally, e.g., on Internet of Things (IoT) devices, will become increasingly relevant, as will federated learning, a machine learning setting in which models can be trained on distributed data. The application of AI systems will occur both from a privacy-enhancing perspective — where the evaluation of data takes place in a decentralized manner — and on IoT devices themselves.

Medical robotics using AI and virtual/augmented reality will continue to evolve. Software tools that support disease diagnoses or therapeutic interventions may be regulated as medical devices, and may create unique regulatory challenges and require new reimbursement/

payment considerations to optimize commercialization and uptake in the marketplace. Continuous data mining by wearables and mHealth devices is well-suited for the application of adaptive AI systems. The conflict between the availability of large amounts of data and privacy/data protection considerations will drive the uptake in the life sciences industry of privacy-enhancing technologies such as homomorphic encryption, multi-party computing, edge AI, and blockchain-based solutions.

Technological advances around wearables and mHealth will increasingly be used to collect RWD for use as RWE in regulatory decision-making. We expect to see an increasing acceptance of RWD and RWE in the drug approval processes, as well as an increase in the use of RWD and RWE in decentralized clinical trials.

In the U.S., the FDA has been undertaking its 21st Century Cures Act obligation to create a framework for the use of RWD in pre- and post-marketing decisions, issuing recent guidance on sourcing RWD from electronic health records and medical claims, addressing the use of RWD in regulatory filings for the approval of therapeutic human and animal drugs, and discussing study design elements and the use of RWD to satisfy post-approval study requirements. Companies have obtained or are seeking approval from the FDA for digital diagnosis and digital therapeutic devices that carry tremendous promise to change care delivery pathways and opportunities in the U.S. European regulators have also launched several initiatives aimed at establishing the position of RWE in regulatory decision-making.

Litigation related to AI and digital health is likely to emerge with more widespread use of these technologies. Life sciences companies operating in these spaces will be looking for ways to minimize risks, and regulatory agencies may well support the development of innovative technology by increasing predictability and transparency.

New regulations that contain requirements specific to AI and digital health are also on the horizon, including China's guidelines for AI-incorporating medical device software, the U.S. FDA's total product life cycle approach, and the proposed EU AI regulation

(which, once adopted, will result in novel legislation), which will provide the legal basis for adaptive AI systems/continuous learning systems.

DIGITAL HEALTH AND AI TIPS:

- Life sciences companies should monitor and map emerging standards and regulatory frameworks.

- Life sciences companies have to be involved in the development of standards.

- There is a need to acquire, and train, a workforce skilled in data science and machine learning.

- The industry needs to embrace responsible and trustworthy AI as the basis for large-scale uptake through the establishment of governance systems, including interdisciplinary governance committees and AI ethics boards.

- Investors and executive teams should understand FDA regulatory and coverage and payment pathways for digital diagnosis and digital therapeutic tools and medical devices, and understand the potential approval and clinical evidence development requirements and compliance obligations associated with such innovation.

- Companies should look for opportunities to minimize risk of tort liability potentially associated with AI and digital health use.

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FDA New Intended Use Regulation: Drug and device manufacturers face significant new risks associated with off-label use of their products

"INTENDED USE" RULE PREDICTED EFFECTS:

Drug and medical device manufacturers in the U.S. have increased potential exposure in off-label promotion cases.

Manufacturers' communications about new uses of lawfully marketed products may not be safe harbored.

There are concerns in the life sciences industry that, in 2022, the FDA's new "intended use" rule will affect manufacturers' safe-harbored communications about new uses of lawfully marketed products in the U.S.

This follows the publication by the FDA, in August 2021, of a final rule amending its regulations defining "intended use." This amendment includes changes that expand the types of evidence that are deemed relevant to determining whether a lawfully marketed drug or device has a new intended use and whether a product is intended for use as a drug or device.

The implications for potential enforcement actions are significant: FDA, DOJ, State AGs, and private parties may assert a new intended use based on purely internal company conduct — for example, brand strategy documents that reflect off-label uses, a product design that makes an off-label use likely or maybe even possible, company-acquired data substantiating the off-label use and analyses of those data, or call plans that include specialists unlikely to prescribe or use the product on-label. On the basis of such evidence, the government could assert a misbranding violation under the theory that the labeling does not provide adequate directions for the new, off-label "intended use." And that could be true even absent direct communications about the off-label use between company representatives and prescribers or patients. DOJ and whistleblowers may, on this basis, take the position that manufacturers have caused the submission of materially false claims for payment to the federal healthcare programs in violation of the False Claims Act.

To assure the immediate implications of the final rule are adequately considered and enforcement risk is mitigated, life sciences companies should consider establishing a cross-functional, senior team representing the key risk management functions of the organization, along with appropriate input from the medical and commercial functions, to consider the degree to which the FDA's approach to intended use potentially affects non-promotional communications of the type that were historically regarded as categorically permissible.

Moving forward, specific proposed activities should be reviewed with a view specifically to assuring that the risk of enforcement under the new intended use definition is adequately considered. That enhanced review should include the company's lawyers in addition to its regulatory affairs personnel.

TIPS FOR MITIGATING RISK UNDER THE NEW "INTENDED USE" REGIME:

- A senior team representing the key risk management functions of the company should consider the impact of the new rule on policies governing nonpromotional communications.

- Legal should be involved in reviewing new proposed activities to assure that the risk implications of the FDA's broader interpretation of intended use are adequately assessed.

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Current Good Manufacturing Practice (cGMP) Compliance: Thoroughness and volume of regulatory inspections are anticipated to increase worldwide

cGMP INSPECTION AND ENFORCEMENT TRENDS:

- Life sciences companies can expect a more robust on-site inspectional effort from regulators worldwide; at the same time, regulators continue to utilize remote-evaluation and record-request tools employed during the COVID-19 pandemic.

- Because of the inspectional backlog due to COVID-19, regulatory authorities are likely to focus their inspectional efforts on sites that:
    + have not been inspected recently and have past cGMP inspectional issues;
    + are critical in the supply chain for important drug products; or
    + have applications pending.

- Manufacturing sites situated in countries with less visibility from corporate headquarters are likely to be particularly vulnerable.

- Life sciences companies are likely to see additional risks arising from regulatory compliance issues.

In 2022, life sciences companies are likely to face a raft of regulatory challenges relating to cGMP: the manufacturing of safe, quality products. We anticipate a more robust inspectional effort from regulators worldwide. This is largely due to the fact that most regulators restricted inspections during the COVID-19 pandemic, resulting in a significant inspectional backlog, and numerous sites around the world that have not been inspected in several years.

Given the fact that significant issues may have arisen in the lag between inspections, investigators are likely to be even more vigilant. Regulatory authorities, meanwhile, will face pressure to verify the companies' systems and the quality of their products. Manufacturing sites situated in a different country from corporate headquarters are likely to be particularly vulnerable, as issues may have developed due to reduced resources during the pandemic, travel restrictions, and the loss of experienced staff.

Regulatory agencies have acknowledged that delays in inspections caused by the pandemic have created backlogs of pending applications because on-site pre-approval inspections of manufacturing sites are required in most instances. The increase of in-person inspections warrants greater focus on inspection readiness, especially because, if problems are found, investigators may not return for longer intervals than they did pre-pandemic, as they work through the remaining backlog (as well as any new backlogs that occur if the pandemic continues). Such delays can impede bringing new therapies to market and disrupt the distribution of existing products, including with regard to attempts to gain approval for changes to optimize current manufacturing processes.

Many agencies are employing new alternatives to on-site inspections, including relying on inspections by other regulatory authorities, conducting remote evaluations, and requesting and reviewing documents remotely. We expect these efforts to continue and to be an overlay to the increased on-site inspections in 2022. Regulatory agencies will also likely offer more regulations and guidance on cGMP in 2022, including efforts to increase focus on critical supply chain sites, especially those with compliance issues,

as well as other areas of changes in the life sciences industry that require analysis and input.

We anticipate that companies will be looking to invest in more reliable sourcing options, with a focus on less-extended supply chains. This may mean investing in retooling existing manufacturing facilities or building new state-of-the-art facilities. It also means updating manufacturing processes through the application of new technology, such as continuous manufacturing models, which would involve utilizing one continuous process to manufacture a product in one facility without hold times, leading to lower manufacturing costs and shorter production times.

It is likely that all companies will face additional regulatory scrutiny with the resumption of significant on-site inspection activities, along with regulators' continued use of remote evaluation and record review tools that were rolled out during the pandemic. Ensuring that manufacturing sites are prepared for detailed on-site inspections — particularly after not having been inspected for years due to the pandemic — will be critical to avoiding the consequences of unsuccessful inspections that can lead to regulatory enforcement, commercial losses from the failure to deliver products, and investor lawsuits related to disclosures. Life sciences companies in particular may experience additional risks arising from regulatory compliance issues, particularly from whistleblowers with regard to issues related to data integrity and product quality, or manufacturing problems related to resource shortages. These issues should be thoroughly reviewed — and addressed if necessary — prior to any regulatory inspection.

cGMP COMPLIANCE TIPS:

- Companies facing inspections should verify that they have executed on prior regulatory commitments and continue to implement robust corrective and preventative actions in response to deviations.

- Life sciences companies that can establish and maintain a reliable supply chain have a competitive advantage.

- Life sciences companies should look to invest in more reliable sourcing options, with a focus on having less-extended supply chains. This may mean investing in retooling existing manufacturing facilities or building new state-of-the-art facilities. It also means updating manufacturing processes through the application of new technology, such as moving toward a continuous manufacturing model.

- Companies should reinforce existing compliance programs and prepare diligently for inspections.

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Privacy: The ongoing trend of new data protection laws and regulations causes new compliance minefields and other legal risks

PRIVACY TRENDS:

In the U.S., privacy and cybersecurity-related enforcement is expected to increase.

In Europe, managing international data transfer restrictions will be a key focus, and additional guidance is expected to be published on areas of digital health such as AI.

In China, new laws and forthcoming guidance will have a significant impact on how life sciences companies process data.

Cybersecurity attacks on life sciences companies are likely to increase.

An uncertain and rapidly evolving data protection landscape means that life sciences companies must pay increasing attention to privacy issues. Data breaches are now more complex, frequent, and impactful, and the cost of these breaches has grown significantly in just the last year.

Policymakers in many countries are having nationwide conversations about data subject rights. Evolving privacy laws pose particular challenges to life sciences companies with global operations, because a major focus of these laws is to regulate cross-border data transfer. Life sciences companies are also being affected by evolving privacy laws across the wider data economy.

In the U.S., regulators are increasingly interested in bringing privacy and cybersecurity-related enforcement actions, and the class action plaintiffs' bar is very active. Preparations for new privacy and cybersecurity requirements that will come into effect in 2023 from state laws in California, Colorado, and Virginia are underway. The development of new regulations in California, and other interpretive guidance or regulators for state laws, as well as potential new HIPAA regulations or guidance, will be a major focus throughout 2022. It is also very possible we will see additional U.S. states pass their own privacy laws during the coming year, and Congress continues to seriously consider federal legislation.

In Europe, issues around data privacy will only become more challenging for life sciences companies during 2022 as concerns around international data transfers continue to evolve. This will create a need to carry out data transfer assessments and put in place new European data transfer agreements. More guidance is expected to be published on areas of digital health, such as AI. Ransomware attacks and other forms of cybersecurity attacks are likely to increase and will be of key concern to life sciences companies.

Last year, China took the major step of introducing a Data Security Law (DSL) and a Personal Information Protection Law. Both impose severe penalties for infractions and will have a significant impact on how life sciences companies process data. In 2022, China is expected

to publish specific regulations and guidance to support the implementation of the new laws. These will include a regulation on security assessment for cross-border data transfer, a China-version standard contractual clause for the cross-border transfer of personal data, and a catalogue of important data that is subject to the DSL.

PRIVACY TIPS:

- As data ethics come more clearly into focus, companies should build data governance programs covering not just existing privacy laws but also extra-legal considerations.

- Life sciences companies should closely monitor U.S. state privacy law developments, as well as distinctions in HIPAA and clinical trial exemptions among state laws.

- In Europe, additional resources will be needed to carry out the required international data transfer assessments and to put in place new European data transfer agreements.

- Life sciences companies with activities in China must closely monitor data privacy regulatory developments. Some data in the healthcare industry may become regulated as "important data," and those processing it will be subject to enhanced security obligations under the DSL.

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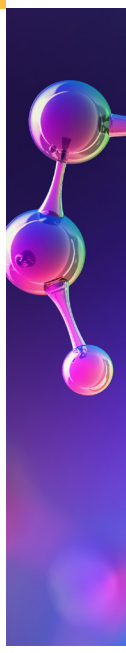
Licensing: Developing combination therapies grows in popularity but creates unique hurdles for partnering agreements

LICENSING TRENDS:

The accelerating pace of the development of combination therapies will increasingly complicate the structuring of licensing agreements.

New regulations around pricing and market access will continue to make partnering increasingly complex.



Combination therapies — therapeutic and diagnostic products that combine different drugs and/or biological products — are on the rise. For example, with the success of new classes of checkpoint inhibitors (a type of immunotherapy used in cancer treatment), research into the health benefits of combining active therapeutics and immune response modulators has accelerated at an astonishing pace and will continue in 2022 and beyond. But just as these therapies are more complicated, so are the partnerships that bring them to market.

A combination therapy creates new pathways to market and potential new uses for a particular compound or biologic. It also introduces new variables that must be considered when structuring the licensing and partnering arrangements. We therefore expect both the pace of partnering and the factual complexity involved in partnerships to increase in line with the accelerating pace of research and development for combination therapies.

Combination therapies pose unique challenges for developers. For instance, the licensing of combination therapies is a very different arrangement from traditional licenses of a single compound for use in a monotherapy. They bring different questions to mind when structuring and create the potential for misalignment of interests between licensor and licensee. For example, because the combination often is targeted to specific disease states and patient populations, the likelihood of indication-splitting increases, meaning the licensee gains rights to the combination for particular disease states rather than for the mitigation or treatment of all diseases. Also, fixed-dose combinations need to be considered carefully for their potential impact on pricing and the allocation of value to the components in the combination. In the year to come, it will be crucial for licensees to be mindful of such concerns when structuring their partnerships.

In 2022, regulators are expected to increase their focus on reducing healthcare costs. This is likely to continue to exert downward pricing

pressure and create increased tension over the allocation of value in a shrinking pool of revenue for a particular therapeutic treatment. As discussed in the Global Drug Pricing section of this report, recently introduced regulations around pricing and market access will also continue to make partnering increasingly complex.

LICENSING TIPS:

- Life sciences companies should consider whether a combination therapy can or will be priced as a single combination therapy, or whether there will be separate pricing for each compound.

- If a generic or biosimilar is introduced as competition to one compound in the combination, the company should consider whether and how this will affect the value of the combination therapy, and by extension, the other compound in such combination.

- If the compound retains significant value and opportunity beyond the initial partnership, companies should think carefully about who controls pricing and market access for the compound. They should also consider the impact of generic or biosimilar competition on each party's right to use data and IP relating to the combination.

- Companies need to remember that the licensee is selling the combination therapy, but may share revenue with the licensor on only one component.

- Life sciences companies need to consider responsibility for market access, pricing, and patient support activities for each compound used in the combination.

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IPOs: New challenges and opportunities ahead for life sciences startups

TOP IPO TRENDS:

Investors globally are taking a more cautious approach toward investing in life sciences and, in particular, emerging growth biotech companies as we begin a new year.

In China, investment will trend toward tech, including life sciences.

We will increasingly see Chinese-founded life sciences startups seeking IPOs in China, Hong Kong, and the U.S.

Looking back on 2021, the number of life sciences IPOs priced in the U.S. is expected to exceed the number in 2020. Recently, the U.S. IPO market has been choppy, with many emerging growth biotech IPOs trading near or below listing price. Many companies and their investors and underwriters are opting to wait until early- to mid-2022, pending more stability in the broader life sciences IPO market. Looking forward, renewed investor interest in 2022 will be dependent on and fueled by sector and asset reallocations, anticipated increased M&A activity, and potentially exciting clinical data and approvals.

Looking to Asia, it has been three years since listing rules reform allowed pre-revenue biotech companies to list on the Hong Kong Stock Exchange. The Hong Kong stock market has emerged as one of the most important listing venues for the life sciences sector globally. The biggest beneficiaries of Hong Kong's nascent biotech scene have been biotech startups and, increasingly, medtech companies. Furthermore, we are seeing U.S.-based and larger global funds investing more in these companies prior to their IPOs.

The IPO market in Hong Kong is now coming back to earth following a high point in 2020, when we saw many life sciences companies fetching high valuations, with stock prices rising sharply during the first day of trading. The biotech market remained extremely busy at the start of 2021, but now, the entire Hong Kong life sciences market has settled down. Investors seem to be taking a more cautious approach, and we expect to see this trend continue throughout 2022.

For years, we saw heavy investment within China in the so-called platform economy, which includes big e-commerce companies. But now China has made the creation and development of its own high-tech companies into a national priority, including through policy measures that support hard science and technology companies. This will prompt investment to trend toward hard-tech, high-end manufacturing, semiconductor chips, and pharmaceutical and biotech. Life sciences will, however, continue to face competition for investment from less heavily regulated sectors.

We anticipate that we will increasingly see Chinese startups seeking IPOs in China, Hong Kong, and the U.S. These will be used to raise capital lifeblood to finance critical research and development for the companies, to reward executives and employees, and also to create exit options for investors and shareholders.

IPO TIPS:

- Issuers and investors should remain nimble. While we continue to see early-stage pipelines generate significant investor and IPO interest, capital markets can remain choppy and investors could pull back, requiring companies to stay private longer.

- Prospective issuers and investors should familiarize themselves with the legal requirements for listing to ensure that their legal structure, financial information, and development programs meet local requirements.

- Issuers should assemble a team of the best scientists, engineers, and leaders, as well as a team of experienced advisers, including lawyers, auditors, and bankers with excellent knowledge of the life sciences market.

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U.S. Special Purpose Acquisition Companies (SPACs): Pursuing a public listing through a merger with a SPAC (a so-called "de-SPAC" transaction) remains an attractive strategy for life sciences companies, despite increased SEC scrutiny and heightened litigation risk

U.S. SPAC TRENDS:

The number of life sciences SPACs is expected to continue to increase, and will be particularly attractive to companies with high growth potential and high capital requirements, like biotechs.

Increased scrutiny by the SEC could result in new proposed regulations impacting SPACs and de-SPAC transactions.

SPACs — public companies formed for the sole purpose of acquiring or merging with another company — are viewed by many as an attractive and alternative road to public markets that offer certain advantages to traditional IPOs, particularly for earlier-stage companies that are pre-profitable or even pre-revenue, but with both high growth potential and capital-intensive growth plans. SPACs are therefore an attractive path to a public listing for the biotech industry, where it can take years of capital-intensive work for drugs to be successfully developed, approved, and marketed.

Although they have been around for decades, SPACs exploded in popularity during the unprecedented market volatility brought on by the pandemic, which made traditional IPOs more difficult to execute due to the way their pricing can unpredictably fluctuate in a volatile market. In the first half of 2021, the number of tech and life sciences companies going public via a de-SPAC merger — the merger of a SPAC and another company — increased by 71% over the second half of 2020, and the number of life sciences de-SPAC transactions quadrupled.

SPACs continued to take the corporate world by storm throughout 2021, showing staying power beyond the volatility seen in the depths of the pandemic. They are expected to remain popular among investors throughout 2022.

There have been some regulatory headwinds, however, that have depressed SPAC activity, and which could contribute to some continued uncertainty for the SPAC market in 2022.

Beginning in the second quarter of 2021, the SEC increased its focus on SPACs, due largely to their newfound prevalence in the marketplace and increased popularity among retail investors as well as traditional institutional players.

First, the SEC threw a wrench in the market by issuing new and unexpected interpretations of accounting rules that required industry-wide accounting restatements by SPACs. Although of

little long-term import to the marketability or viability of the SPAC product, the sudden change created massive bottlenecks in the SPAC ecosystem, which depressed deal activity almost overnight.

At the same time, senior SEC officials began making what have now been numerous public comments calling into question the strength and effectiveness of the current rules and regulations applicable to SPAC IPOs and de-SPAC mergers, waxing philosophical about the divergence between the rules governing de-SPAC mergers versus traditional IPOs, as well as a potential divergence in perceived investor protections offered between the two.

Historically, companies going public through a de-SPAC have been able to take advantage of rules governing merger transactions, including safe harbors from certain lawsuits that have served to protect de-SPAC participants from otherwise costly securities litigation. That, in turn, has facilitated the now almost universal use of a de-SPAC target company's forward-looking financial projections to promote its de-SPACs in a manner not facilitated by the rules governing a traditional IPO. The use of such projections has been a critical distinction from — and for many companies choosing to de-SPAC, a key advantage over — traditional IPOs.

The public statements by senior SEC officials calling this regime into question has led many to fear that new rule proposals and interpretive guidance are in the offing for 2022 that could in some way quell the use of such projections and thus have a chilling effect on the SPAC market as a whole.

However, it is unclear how and when any rule changes would be implemented, and whether the SEC would have the authority to do so in a manner that could fundamentally alter, or in the worst case grind to a halt, the SPAC market without legislative action. All eyes will be on the SEC in the coming months to see what, if any, new SPAC regulations they may propose.

U.S. SPAC TIPS:

- SPACs remain a viable path to access the public markets and raise critical financing for life sciences companies in 2022, despite some regulatory headwinds. Companies should be prepared to execute quickly and effectively should they see the opportunity to take advantage of the de-SPAC process to go public.

- Life sciences companies should beef up internal audit functions, prepare management and employees for public company-style quarterly disclosure and 24/7 public accountability, prepare two to three years of audited financial statements, develop robust business plans and financial projections, and do a thorough housecleaning to understand how their financing history, organizational documents, and other contractual relationships could impact the timing and success of a possible de-SPAC transaction.

- Robust due diligence by SPACs and target companies, thorough and rigorous public disclosures in the de-SPAC registration statement, and the implementation of structural legal measures to cleanse any potential conflicts of interest that may exist between de-SPAC participants and public SPAC shareholders should all be considered in order to mitigate both increased regulatory scrutiny and resulting litigation risk in de-SPAC transactions.

Contacts

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Antitrust and Competition: Enforcement scrutiny of M&A and licensing deals in the U.S. and EU focus on "excessive pricing" expected

ANTITRUST AND COMPETITION TRENDS:

Enforcement actions and investigations are likely to accelerate in relation to M&A and pricing and distribution.

More "excessive pricing" cases are expected to be brought in the life sciences sector.

International cooperation on life sciences deals between national antitrust agencies will likely increase.

We have recently seen heightened enforcement against life sciences companies. Far from dying down, this enforcement activity is likely to accelerate over the coming year. National antitrust regulators such as the U.S. Federal Trade Commission (FTC) and the UK Competition and Markets Authority (CMA) will likely increase their activity, particularly in relation to M&A transactions and pricing and distribution practices.

Life sciences companies should therefore expect to see more conduct investigations and lengthier, more intrusive M&A reviews. In multi-company situations, such as M&A and IP licensing, these are likely to put stress on the allocation of regulatory risk and complicate the ability of the parties to reach agreement.

In Europe, more life sciences M&A deals involving high-value but low- (or pre-) revenue targets may be referred to the European Commission. The Commission may also pursue additional "excessive pricing" cases in the life sciences sector. At a transatlantic level, cooperation and exchanges of information between national antitrust agencies on life sciences deals are likely to increase throughout 2022. This follows the move in March 2021 by the Competition Bureau Canada, the FTC, the U.S. Department of Justice, the CMA, and the European Commission to create a multilateral working group that analyzes the effects of mergers in the pharmaceutical sector.

These developments will create particular opportunities for investors in the M&A area. First, antitrust considerations may give financial investors an advantage if they have a limited existing footprint in a particular product. Second, the risk associated with antitrust considerations has value. In any given transaction, whichever party is able to more accurately assess the risk will be able to pocket a disproportionate share of the value. Third, M&A deals in the life sciences sector are perhaps more likely to be approved only conditionally (or subject to consent decrees). Therefore, forced divestments of products or pipeline products will create opportunities for potential buyers of the assets to be divested.

ANTITRUST AND COMPETITION TIPS:

- Life sciences companies should identify any corporate practice that could be vulnerable to antitrust laws, determine whether the exposure for this specific practice has the potential to be severe, and look for resources to mitigate the risk.

- For example, in the M&A area, life sciences companies should determine early in the process whether a transaction presents any material risk of extended investigation or possible intervention. Then, unless the counterparty is prepared to assume all risk, the company may want to consider a detailed antitrust review.

- Life sciences companies should ensure that compliance, training, and document management policies and procedures are up to date and reflect the increased enforcement focus on pricing and distribution issues. These good practices should continue in the M&A evaluation phase.

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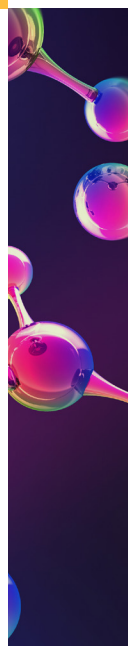
Private Equity (PE) Investor Risks: PE funds invested in U.S. life sciences companies face enforcement actions for portfolio company misconduct

PE ENFORCEMENT TRENDS:

In the U.S., both the government and whistleblowers increasingly are pursuing PE investors in False Claims Act (FCA) cases based on alleged violations of healthcare fraud and abuse laws.

Both majority and minority investors are exposed to this FCA risk.

PE funds face increased risk in 2022 as the U.S. Department of Justice (DOJ) renews its focus on curbing perceived fraud and abuse in the life sciences industry and as government scrutiny of PE investment in the sector increases.



In 2022, PE funds should expect the DOJ and whistleblowers to continue to assert claims against them relating to the conduct of their life sciences portfolio companies. This risk will continue to be of concern to PE firms that are active in the operations of their portfolio companies and may be of concern to all firms that identify potential issues of noncompliance during diligence and, if they assume managerial responsibility, do not take steps to ensure appropriate actions are taken to bring operations into compliance.

Across the board, PE funds may find themselves at further risk as DOJ enforcement scrutiny of actors in the life sciences industry, including equity investors, in the U.S. ramps back up to pre-pandemic levels in 2022. Enforcement priorities are predicted to include:

- federal Anti-Kickback Statute issues implicated by provider referral source arrangements, compensation by drug and device manufacturers of contract sales forces, and rebate arrangements with pharmacy benefits managers;

- issues related to promotion of products for new intended uses in alleged violation of the Food, Drug, and Cosmetic Act and violations of current Good Manufacturing Practice regulations; and

- issues related to CARES Act funding and the Provider Relief Fund.

PE funds invested in the healthcare and life sciences industries should stay up to date on the latest enforcement trends to calibrate their investment opportunities and to manage risk in their portfolios.

PE ENFORCEMENT TIPS:

- Funds need to be attuned to the specific areas of high-priority enforcement risk facing their life sciences portfolio companies.

- PE firms should ensure that their portfolio companies are resourced for sound compliance programs and there is a documented process for board oversight.

- PE firms should follow up on issues of noncompliance identified during diligence and document that follow-up.

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IP Litigation: A new battleground for patents is forecasted based on innovations in medtech software and biologics

IP LITIGATION TRENDS:

There is likely to be a move away from patent litigation over mechanical devices toward medtech software innovations.

We anticipate more litigation around non-practicing entities and more litigation involving biologics.

In medical devices, the patent litigation battleground is moving away from mechanical devices toward litigation around medtech inventions that rely heavily on software implementation. In light of the significant innovation now occurring in the medtech sector, the primary objective of IP litigation is often the increase of market share.

With the significant growth of medtech inventions, there is an expectation that non-practicing entity (NPE) litigation — claims brought by entities that acquire patent rights but do not offer products or processes on the market — will also rise in the life sciences industry. Until now, NPE activity in medtech has remained remarkably low, just 23.3% of all cases from 2015 to 2021 (compared to 60–90% in other industries), according to a recent article on IAM. But as the medtech sector continues to achieve growth and profitability, NPE litigation is expected to increase.

We expect to see an increasing risk of patent invalidity under 35 U.S.C. §101 for lack of subject-matter eligibility, another import from the high-tech industry. As in the high-tech industry, we expect more medtech companies to turn to protecting their software innovations as trade secrets rather than publicly disclosing them in patent filings.

The increase in medtech litigation will impact both large, established players and smaller startup companies looking to gain a foothold in traditional markets. Smaller startup companies often tend to have innovative products and are looking to disrupt markets. This presents challenges to established companies, which fuels competitor litigation. Companies will need to increasingly prepare for inevitable litigation sooner and focus more on protecting their markets.

We also anticipate an increase in litigation in the biologics area, as pharmaceutical companies look to develop and bring to market products including biosimilars. This is likely to be particularly marked among big pharma companies, and will to a lesser extent affect biotech startups. One factor driving this type of litigation is the historically broad scope of biologics patents, which creates bona fide patent invalidity issues: for example, in relation to

patent "enablement," meaning whether a patent makes sufficient disclosures to enable a person of skill in the art to make and use the invention. But those considering embarking on biologics should bear in mind that many biologic patents have encountered effective challenges in litigation.

IP LITIGATION TIPS:

- Medtech companies should:
  - + ensure that their patent portfolios are sufficiently robust, so that they can pursue infringers and protect patents defensively if sued by a competitor;
  - + put robust confidentiality provisions in their employment agreements and separation agreements; and
  - + implement strict measures to protect their software innovations as trade secrets where possible, such as encrypting where necessary, and ensuring that disclosure is made only on a need-to-know basis within the company.

- In the biotech field in particular, patents should be written in a manner that better withstands enablement scrutiny. This includes having claims that are commensurate in scope with the patent disclosure.

- Investors should look for companies that have a robust patent portfolio, which can be used to create new market opportunities and defend existing markets.

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Arbitration: The fallout from a wave of disputes since the initial COVID-19 outbreak will ricochet over the coming year

ARBITRATION TRENDS:

Expect to see an increase in disputes over earn-out clauses in M&A transactions and third-party funding of significant claims in arbitration.

It is also likely that there will be a rise in investor-state claims alleging breach of international investment protection agreements.

Paperless proceedings and video hearings are here to stay.

Insolvent parties in arbitrations will increasingly be a problem.

We anticipate seeing an increase in disputes that have, directly or indirectly, been caused by COVID-19. The pandemic greatly increased the costs of transportation and certain raw materials, complicated the manufacturing of drugs and medical equipment, and generally affected international trade.

Urgent demand for certain products resulted in an increase in complaints about inferior products entering the market and being rejected by customers. We saw governments taking a keen interest in diversifying supply chains in order to ensure a reliable and secure supply of materials over the longer term. Some governments pushed for new, domestic sources of supply. They directed exporters to prioritize new local or national needs over fulfilling their contractual obligations with overseas customers. All of these factors triggered disputes. We also saw disputes arising as life sciences companies restructured their supply networks or sought price adjustments, and defenses such as force majeure or hardship increased.

M&A transactions have included more earn-out components to address the uncertainties arising from the pandemic by linking part of the purchase price to the company's future performance. In the future, we anticipate an increase in disputes over earn-out clauses, which are often resolved through arbitration.

The pandemic also accelerated the need for innovation, with manufacturers and governments working to expedite advanced critical drug development. At the same time, we saw increased tension between the need to protect the legitimate IP rights arising from innovation and the need to expand access to IP. In some instances, governments led the charge to make critical drugs widely and cheaply available, even to the extent of overriding existing licensing arrangements and underlying patent protection. These will likely give rise not just to contractual breach claims, but also to investor-state claims alleging breach of international investment protection agreements.

Third-party funding of significant claims in arbitration is now a common feature in international arbitration and has become available in more

jurisdictions that previously were subject to regulatory restrictions. These funding arrangements are anticipated to increase further. They will also offer interesting options for investors, who might want to consider the option of putting money into third-party funding of cases in the life sciences sector. The increased availability of third-party funding creates opportunities for life sciences companies to consider utilizing such options to help manage their litigation budgets.

In 2022, we anticipate that arbitral tribunals will more frequently need to address the issue of parties having financial difficulties or becoming insolvent, and the possible consequences for an arbitration. Issues that may arise include security for costs orders, the question of whether an insolvent company still has standing to sue or to be sued, delays in proceedings to determine who has authority to act for an insolvent company, etc.

ARBITRATION TIPS:

- Life sciences companies should consider whether available third-party funding options could help manage their litigation budgets. This decision requires careful weighing of the advantages and disadvantages of third-party funding, such as a limited cost exposure versus ceding to the funder some degree of control and a significant part of any amounts won.

- Investors are increasingly putting money into third-party funding of cases in all sectors, including life sciences.

- Life sciences companies should carefully consider the financial standing and risk of insolvency of their counterparty before initiating legal proceedings.

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