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Life Sciences 2022

USA: Trends & Developments

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Trends and Developments

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New Trends and Developments in Life Sciences

Over the past two years, the COVID-19 pandemic has had a profound impact on the life sciences industry. In many cases, the pandemic accelerated change already under way, and in other cases reoriented it, giving rise to a surge in collaborations, increased adoption in decentralised clinical trials and a shift towards supplier diversification. Today, many life sciences companies are more collaborative, more digital and more focused on pandemic preparedness than they likely would have been without the pandemic. As the pandemic turns endemic and new variants emerge, emerging trends and developments in the biotechnology, pharmaceutical, medical device and digital health sectors for the year ahead will be examined in this article.

Biotechnology

Biotech investment activity reached record levels in 2020 and 2021, but the outlook for 2022 remains uncertain. In 2021, large amounts of capital flowed into the industry through venture financings, initial public offerings (IPOs) and de-SPAC (SPAC – special-purpose acquisition company) mergers. Newly public biotech companies debuted on public markets through 78 traditional IPOs and 13 SPAC IPOs, raising an estimated USD14 billion. However, in 2022, biotech companies are encountering a more competitive public financing market. The benchmark biotech exchange-traded funds (ETF) ticker, XBI, started the year down 25%. Nearly 80% of the class of 2021 IPO companies are trading below their offering price. As of mid-February 2022, there have been just 13 IPOs and two SPAC IPOs, significantly fewer than from the same time last year, and an indicator of slower investment activity. This year, deal activity will likely remain strong for licensing and collaborations, and M&A activity may increase as biotech companies seek alternative exits to public offerings. In addition to the macro-economic factors affecting markets, biotech deal activity is also likely to be impacted by regulatory risk and operational issues.

Despite a slow start in new investment activity in 2022, the number of licensing and collaborations between biotech companies, including partnerships between biotech and large pharmaceutical companies, are expected to remain robust. This includes the traditional worldwide, all-fields licensing and collaboration deals, but also more regional licensing, co-development and co-commercialisation deals. There are a few primary drivers of this trend. First, weakness in the capital markets has caused biotech companies to delay going public and instead to partner-off assets in order to raise cash in what used to be considered non-dilutive financings. Further, large capital inflows over the past few years have allowed some biotech companies to develop products independently to a later, more de-risked stage that is likely to be more attractive to potential large pharmaceutical partners. Finally, the continuing rise of platform technologies also contributes to the strong number of discovery-stage partnership deals. Such technologies have broad applicability, which lend themselves to many licensing deals with a narrowly defined scope.

Biotech M&A deal activity in 2022 will likely increase from last year, but it is too early to tell to what degree this will happen. M&A will appeal to

established pharmaceutical companies looking to add later-stage assets. Lower biotech company valuations will further facilitate deal-making this year. Pharmaceutical companies with strong cash-flows from successful COVID-19 therapies and vaccines are also expected to add to and diversify their pipelines through strategic mergers. One factor that may suppress biotech M&A activity is an unwillingness of biotech boards to approve a merger. This is particularly likely in an environment where board members believe stock values are temporarily depressed and where the company has sufficient cash to weather the rocky financing markets.

Although not as common in recent years, it is expected that more reverse-merger activity in the biotech space will be seen, due to the uncommon situation of many newly public biotech companies and comparatively low valuations. A number of biotech companies are trading below cash value, meaning companies have more cash on hand than the company's market capitalisation. These companies are attractive acquisition targets and create an environment ripe for reverse mergers, in which a private company becomes a public company by purchasing control of the public company. The private biotech company potentially adds to its drug pipeline from the acquisition and obtains the public biotech company's cash, potentially with a concurrent private investment in public equity (PIPE) financing to bolster the balance sheet further.

Increased federal regulation may play a role in biotech deals in 2022, particularly with respect to the fast-growing Chinese biotech market. US-China trade tensions have continued to be an ongoing issue. Since the start of the pandemic, governments across the world have also moved to more protectionist postures with respect to domestic healthcare industries. More recently, the US federal government added two subsidiaries of WuXi Biologics – a prominent Chinese contract development and manufacturer – to its Unverified List. The Unverified List is a list administered by the Bureau of Industry and Security (BIS) within the US Commerce Department. For a party on the Unverified List, export licences are required to transfer certain items to that party. The Unverified List designation is not as expansive as other methods the federal government uses for restricting exports; however, it does impose additional restrictions. US companies engaging in deals with a party on the Unverified List that require a transfer of materials should be aware of the restrictions and take appropriate steps to comply with regulations. An environment of increased biotech trade scrutiny, combined with a recent Department of Justice crackdown on foreign researchers in the US, presents more uncertainty and regulatory risk for US-Chinese biotech tie-ups.

Operational issues, including supply chains, will remain a focus for biotech in 2022. Amidst supply-chain uncertainty, biotech companies continue to search for alternative sourcing options and assurances of supply in existing supplier relationships. Digital supply chains have increased transparency, aiding in companies' planning ability for continuity of supply. However, growth in personalised medicine, such as cell and gene therapies, has further pressured supply chains. These therapies require more sophisticated supply chains because of the individualised treatments and the nature of the products, including sensitivity to environmental factors, specialised storage and time constraints.

Another operational challenge biotech companies continue to face is talent acquisition and retention, particularly in the ranks of top executives. The supply of talented individuals has not kept pace with the industry's growth, and the battle for talent has driven up compensation packages significantly. The number of individuals moving from academic research to industry

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also reflects this demand for talent, as many look to translate their research knowledge toward the pursuit of new commercial therapies.

Pharmaceuticals

The pharmaceutical sector is emerging from the pandemic with new techniques and innovations. The success of the mRNA-based COVID-19 vaccines has inspired developments, both with new target diseases and new methods of delivery. Already, three major companies – Moderna, Pfizer, and Sanofi – have begun clinical trials of mRNA-based vaccines for influenza. In late February, Moderna announced three new mRNA vaccine targets, including herpes simplex, varicella-zoster virus, skin cancer and non-small cell lung carcinoma. Pfizer, too, is researching mRNA vaccines for varicella-zoster. Progress is visible, not just in targets of mRNA vaccines but also their delivery. The cold-storage requirements for mRNA vaccines posed a problem throughout the pandemic, but in late February, MIT researchers reported preliminary success with an mRNA vaccine swallowed in pill form.

Nevertheless, this focus on mRNA vaccines furthers the division between those with access to medicine and those without. Many countries struggled to obtain supplies of mRNA vaccines for their citizens, and even when they did, the cold-storage conditions required proved a logistical challenge. In mid-February, the WHO said it would work with six countries in Africa to receive the technology required to produce mRNA vaccines in the hope of boosting global accessibility. In this announcement, WHO chief Tedros Adhanom Ghebreyesus warned that reliance upon a small number of powerful companies to supply necessary goods is “limiting and dangerous.”

This emphasis on global production of vaccines lays the groundwork for the growing market sector of pandemic preparedness. Companies and governments alike are ensuring that, when and if the next pandemic strikes, they will have the ability rapidly to produce mRNA-based vaccines independently and not need to rely on others. National Resilience, a company led by former Novavax CEO and COO of Takeda Vaccines, brands itself as specialising in bio-pharmaceutical manufacturing preparedness in the face of disruption. Having only launched in 2020, it has already amassed USD800 million and acquired several laboratory facilities. Moderna has announced a vaccine-production partnership with the Canadian government, using National Resilience’s Ontario facilities as a manufacturing base, as well as a separate partnership with the Australian government towards building an mRNA manufacturing facility in Victoria. Many in the field expect that these types of partnerships will increase as more countries aim for self-sufficiency in the face of disaster.

Tempering the heady rush of vaccine success is the depressed rate of clinical trial enrolment, which has fallen since 2020. As one source reports, 80% of current trials do not enrol within target enrolment timeframes, and 55% of terminated trials cite low patient enrolment as the primary reason. The scientific community is beginning to report data on just how depressed rates have been. In lung cancer clinical trials, enrolment declined 14% worldwide during the pandemic. The pandemic impacted every aspect of enrolment, resulting in lower numbers of eligible patients, a decrease in protocol compliance, institutional suspension of trials and patient inability to travel to sites due to travel restrictions or fear of on-site infection.

Nevertheless, researchers are finding creative ways around lowered trial enrolment: clinical trials are increasingly being conducted remotely. Rather than relying upon physician recruiters at academic hospitals, large companies increasingly manage subject outreach and recruitment independently. Furthermore, principal investiga-

tors are relying upon improved machine learning as a tool of both enrolment and experimentation, to manage clinical trial matching and to operate on large data sets. Moreover, in pursuit of larger and more representative samples, researchers are using novel recruiting methods to target under-studied populations. Would-be subjects in geographically rural areas, who formerly could not travel to academic medical centres in cities, can now be reached via trials run in national pharmacies, online, or via telehealth or even home-nursing visits.

Despite their promise, decentralised clinical trials present problems integral to the nature of remotely conducted studies. First, failing to ensure standard format and delivery potentially introduces noise into experimental set-ups, particularly for behavioural interventions. In addition, certain kinds of measures cannot be collected remotely. Furthermore, researchers operating in this fashion have found it "burdensome" to upload staggering data files to be shared virtually. Regulatory concerns are also afoot, from worries about the cross-state practice of medicine to oversight of at-home clinician visits. Shipping drugs across state lines has posed concern as well, although shipping companies such as Amazon have begun obtaining pharmacy licences in multiple states. Despite these concerns, some are calling remote-trial enrolment a new standard. It is expected that more researchers will make use of this tool, where appropriate, in the coming years. As this unfolds, a reckoning between the ease of remote trials to obtain larger and more representative sample sizes, on the one hand, and the challenges of standardising experiments, on the other, is predicted. Remote trials may prove better adapted to certain fields of research than to others.

Under the public's watchful gaze, the FDA has been slowly returning to normal, though delays are still rampant. In 2021, the FDA's Center for Drug Evaluation and Research approved 50 novel molecular entities and therapeutic biological products. This may represent a return to pre-pandemic times; the onset of the pandemic caused novel drug approvals to dip from 59 in 2018 to 48 in 2019, with 2020 showing stabilisation at 53. The five-year average approval for novel drugs is 51 drugs per year. 2021 was also a year when the FDA periodically missed review deadlines. Whereas the FDA reviewed 98% of Prescription Drug User Fee Act (PDUFA) applications on time in the third quarter of 2020, that figure was only 91% for 2021, sometimes significantly setting back companies' development plans. These delays arguably represent a shift away from the period of emergency-use authorisations and back to the methodical evaluations for which the agency is known – and to a focus on conditions other than COVID-19.

As pharmaceuticals and their production become more complex, the somersaults involved in pharma licensing also evolve. Emerging modalities, such as mRNA and gene editing, involve many sources of intellectual property that must be in-licensed and that cover numerous areas of the product. Practitioners have seen an increased focus in transactions upon manufacturing relationships, as well as more royalty-stacking. Increasingly, sub-licence income clauses of collaboration or licensing agreements spur litigation and arbitration to interpret their sharing provisions.

Despite these developments, the attitude coming out of the recent J.P. Morgan Conference, as well as that reported by numerous practitioners, is that the pharma sector is returning to business as usual. Overall indications are that the sector may return from the pandemic to an even healthier state than before, with a better public reputation and more innovative research techniques and products.

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Medical Devices

Global supply-chain challenges caused by the COVID-19 pandemic continue to raise concern for medical device companies and are likely to persist in 2022. With the anticipated emergence of new COVID-19 variants, government authorities may continue to impose certain restrictions, such as closing shipping ports, which may lead to disruptions and logistical challenges for medical device companies, especially those that rely on foreign suppliers.

The medical device sector is further burdened by increasing inflation rates for raw materials and a shortage of critical materials, such as semiconductor chips. Medical device companies are likely to continue diversifying their supplier networks by establishing relationships with multiple vendors. In the context of mergers and acquisitions, parties may address potential supply issues by including interim operating covenants that would allow the seller to respond to potential supply-chain disruptions by taking actions outside the ordinary course of business. The FDA has also taken action to combat supply-chain issues by dedicating USD21.6 million of its fiscal year 2022 budget to establish the Resilient Supply Chain and Shortage Prevention Program (RSCSPP) in the Center for Devices and Radiological Health (CDRH). The RSCSPP is charged with fortifying the domestic medical device supply chain through preventive action, expeditious interventions, continual monitoring, and review and discovery of potential deficits.

The demand for certain classes of medical devices has varied significantly due to the ever-changing healthcare system during the pandemic. With respect to COVID-19 diagnostics specifically, the demand for both clinic and at-home tests skyrocketed and shows no sign of abating. Demand for remote monitoring devices continues its positive trend, with the emergence of new wearable devices that provide patient health data to healthcare-providers remotely. In contrast, the demand for certain orthopedic and cardiovascular devices has temporarily declined in certain geographies, due to the re-establishment of moratoriums on certain elective procedures.

Outside the US, new EU regulations such as the Medical Devices Regulation (MDR) and In Vitro Diagnostics Regulation (IVDR) are expected to have a significant impact on the business models of medical device companies in Europe. The IVDR, which comes into effect in May 2022, replaces the current In Vitro Diagnostic Directive and modifies the regulatory framework for in vitro medical devices and the approval process for obtaining CE-mark and marketing products in Europe. Specifically, the IVDR calls for increased activity by conformity assessment bodies used to monitor device compliance independently prior to such a device reaching the European market. Under the IVDR, approximately 80% of in vitro diagnostic medical devices, as opposed to 20% under the prior directive, will be subject to conformity assessment bodies. The IVDR's more complex requirements and anticipated lengthier approval process may alter the strategy medical device companies use to launch products – from launching first in Europe, to the US instead. The MDR, which came into effect last year, also introduced more complex regulatory requirements for both new and existing medical devices in the European market by requiring more detailed technical documentation provided with devices. The MDR is challenging because of the increased resources and costs needed to meet medical device compliance, which some surveys estimate could result in expenses between 5% and 10% of a company's annual revenue. This added expense may necessitate that certain medical device companies, particularly those smaller or less prepared, will have to offset these costs elsewhere, which may include delaying or terminating new product offerings.

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Digital Health

2021 was a record-setting year in digital health, with funding of nearly USD30 billion across over 700 deals and over 270 M&A transactions. It is expected that interest in digital health and health IT tools will only continue in 2022, as changes precipitated by both the COVID-19 pandemic and the increased interest of consumers in managing their own health are likely here to stay.

Development and adoption of digital health innovations are accelerating, in large part due to a persistent shortage of physicians, nurses and other skilled healthcare workers. The pandemic has exacerbated pre-existing stressors in the medical field, leading to widespread burn-out, turnover, rising salaries for nurses, and a failure to return to pre-pandemic rates of treatment and utilisation for many conditions. Even as the Omicron wave has peaked and case rates are dropping, it is unlikely that personnel shortages and the increased costs associated with retaining staff will decrease, leaving healthcare systems scrambling for methods to increase efficiency and deliver asynchronous remote care.

While telehealth utilisation rates have dropped from their peak during the first six months of the pandemic, rates are still significantly higher than pre-pandemic. Multiple states have allowed their public-health emergency (PHE) declarations to lapse, and with them executive orders which permitted out-of-state professionals to offer telehealth services to state residents. Some states have since issued new PHE declarations and reinstated licensure waivers, while other states such as Arizona, West Virginia and Connecticut have enacted laws making regulatory waivers surrounding telehealth enacted during the pandemic permanent. The continued growth of the Interstate Medical Licensure Compact, which currently includes 33 states, the District of Columbia and Guam, creates increased flexibility and opportunities for licensure by out-of-state professionals.

There is also a Congressional push for making Medicare telehealth expansions permanent, a move which would greatly decrease uncertainty for telehealth providers. While telehealth providers will need to monitor evolving trends in licensure and regulation continually, telehealth will continue to be an important and lucrative treatment modality.

Also continuing from 2021 is an increasing convergence of medical devices, mobile apps and wearables. Increasing consumer demand for health and wellness technologies not only expands the market for these medical devices, but also the valuable digital biomarkers collected by these devices and programmes. As the data collected, stored and analysed by firms becomes even more voluminous, so does the value of these databases and associated risks. Cybersecurity and data privacy will be top concerns for firms in 2022, especially considering regulatory initiatives, such as the Federal Trade Commission's (FTC's) intention to enforce the Health Breach Notification Rule against non-HIPAA regulated entities.

Many of these new wearables, medical devices and mobile apps will include elements of both artificial intelligence (AI) and machine-learning (ML) technologies. As these technologies are increasingly utilised, new regulations from the FDA will help clarify the legal landscape. Important developments expected by the end of the year include draft guidance on Clinical Decision Support Software, as well as more general FDA guidance on the development of AI and ML functions by the FDA Digital Health Center of Excellence.

The greater prevalence of wearables and mobile health devices will also increase urgency for the

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FDA to finalise a framework for the use of real-world data (data generated outside of clinical trials by doctors and patients), as mandated by the 21st Century Cures Act. The FDA has showed increased comfort with real-world data collected during the pandemic to evaluate potential treatment options and has already released two documents of draft guidance for the use of real-world evidence for drug and biological products. Devices used to collect real-world data and the AI-based systems used to analyse that data will drive growth in the digital health space and offer firms looking to bring drugs and biologicals to market new methods of gathering data for regulatory approval.

It is expected that digital health innovations will rely on continued advances in inter-operability and security in cloud platforms, which enable the secure transfer and sharing of healthcare data. Systems that enable the secure collection and dissemination of data for use in remote decentralised trial designs, training of AI and ML programmes and the creation and maintenance of patient records that can be easily accessed across platforms will continue to pose complex legal and regulatory issues. US regulatory regimes are only one part of this tapestry; given the desire of many firms to operate in the European Union, ensuring that new and rapidly evolving digital health data collection and analysis platforms comply with the General Data Protection Regulation (GDPR) will continue to be vital. Firms will need to continue taking measures to protect against ransomware, conduct cybersecurity risk analyses and ensure that individuals have access to their electronic health data.

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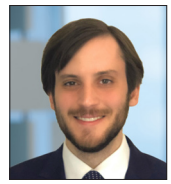

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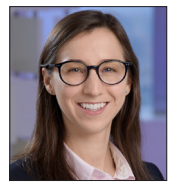

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