King & Spalding
Client Alert

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Pharma Investment Trend Report: What We're Watching in 2023

2022 was a big year for the pharmaceutical and biotechnology sectors. Novel technologies emerged at a rapid clip. The Food and Drug Administration ("FDA" or the "Agency") approved over forty novel drugs and biologics and published guidance and issued rules on topics ranging from wholesale drug distribution licensing standards[1] to over-the-counter drugs with additional conditions of use.[2] The ripple effects of court cases continued to be felt,[3] and Congress enacted the game-changing Inflation Reduction Act[4] and the next iteration of user fees[5] (even salvaging some of the earlier bills' policy riders in the Consolidated Appropriations Act, 2023[6]). While COVID-19 continues to shape FDA's priorities, 2023 will also herald new trends.

Cell and Gene Therapies

Cell and gene therapies had a banner year in 2022. We expect the exponential explosion in cell and gene therapy product development to continue on this upwards trajectory. FDA expects this too—the Center for Biologics Research and Evaluation reorganized key offices to facilitate engagement on these products,[7] supported by a major new funding stream.[8]

We'll be keeping an eye on:

- How FDA uses accelerated approval for cell and gene therapies, especially in the wake of controversial, high-profile accelerated approvals of other drugs
- Dueling stem cell clinic cases in California and Florida regarding FDA's authority over certain kinds of stem cell products[9]
- Whether the dominance of therapeutic cell and gene therapies will create opportunities to push for jurisdiction when the different culture and practices of one Center over the other better suits a particular product

Biologics and Biosimilars

We expect drug development and market share to continue to shift towards biologics, especially given these products' preferential treatment under the Inflation Reduction Act. At the same time, biosimilars (follow-on biologics) have taken center stage, with 2023 anticipated to serve as an inflection point for the industry.

We'll be keeping an eye on:

- Publication of the inaugural list of selected drugs under the Inflation Reduction Act, and the likely viability test of the "Special Rule for Biosimilars"[10]
- The hotly anticipated launch of numerous biosimilar and interchangeable products in 2023, and the impact of this entry on the market
- The possibility of biosimilar cell and gene therapies, and other, novel biosimilar drugs
- Decreasing data requirements for (and corresponding increasing numbers of) interchangeable applications and approvals. Only one of the four interchangeable products approved by FDA to date has included additional clinical data beyond what was required for biosimilarity

Complex Combination Products and Biologic Delivery Devices

Drug products have become increasingly complex, particularly with respect to delivery devices. Additionally, new formulations and technologies (both drug- and device-related) further open the door to innovative delivery device opportunities. With the Agency classifying more and more products as combination products, we expect 2023 to witness continued rapid growth in this area.

We'll be keeping an eye on:

- A slew of expected combination products guidances promised by the FDA's Office of Combination Products, on topics ranging from cross-labeled combination products to postmarket changes, emergency-use injectors, and insulin pumps
- How FDA handles a statutory gap that make these kinds of innovations difficult and inefficient for biologics—specifically the difficulty biologics manufacturers have leveraging FDA's finding(s) with respect to other drugs as safe and effective to support approval. FDA may seek a more flexible approach to differences in devices between a biosimilar and its reference product
- Increased scrutiny over FDA's recent change in classification of ophthalmic products with both simple and complex dispensers[11]

Digital Health Tools and Prescription Drug Use-Related Software ("PDURS")

Digital health and telemedicine innovations like telehealth portals, devices with Bluetooth connectivity, use of digital health tools in clinical trials, and software tools intended for use with prescription drugs are all expected to continue surging in the upcoming year.

We'll be keeping an eye on:

- FDA's heightened sensitivity to data privacy issues arising out of increased use of digital health tools, especially software
- FDA's new, more aggressive approach to Clinical Decision Support Software,[12] which will face intense scrutiny and possible legal challenges
- New guidance and information regarding the regulation of PDURS, including the potential treatment of PDURS output as promotional or required drug labeling

Real-World Evidence ("RWE")

FDA has been increasingly confronted with (and willing to consider) RWE in regulatory decision making for drugs. New statutory authorities[13] and experience with RWE during the COVID-19 public health emergency will also continue to drive use of RWE by drug developers and regulators.

We'll be keeping an eye on:

- FDA's increasing openness to RWE, with a number of user fee commitments made to support digital health technologies[14]—particularly in the untapped premarket arena
- The growth of ancillary and regulation-adjacent services, as the digital health revolution generates rich data sources, including from patients outside clinical trial settings
- The creation of potential new sources of RWE from digital health tools for clinical trials, which, in conjunction with enhanced computing power and more sophisticated analytics, may help with innovative modeling and data validation systems

Early-Stage Oncology

Historically, accelerated approval in the oncology space has focused on late-line therapies, both because later line therapies represent an urgent unmet medical need for patients who have exhausted all other options and such later line indications often involve less expensive, smaller single-arm trials. FDA has recently been pushing industry to think earlier, encouraging focus on neoadjuvant treatments and other early-stage treatments.

We'll be keeping an eye on:

- The launch of FDA's Project FrontRunner, through the Oncology Center for Excellence, which seeks to encourage the development of new cancer drugs in earlier clinical settings supported by randomized, controlled clinical trials[15]
- FDA's dedication of increased resources to refocusing the oncology development model more broadly, including with respect to dose ranging and lower-dose trials, as well as biomarker development

Artificial Intelligence ("AI") Manufacturing

The executive branch has taken a keen interest in advanced manufacturing. President Biden launched the National Biotechnology and Biomanufacturing Initiative,[16] prompting the Department of Health and Human Services to publish its plan to support the development and implementation of advanced manufacturing technologies.[17] FDA has also promised a public workshop on the utilization of innovative manufacturing technologies.[18]

We'll be keeping an eye on:

- The continued development of AI technologies to expedite and optimize drug candidate design and selection as well as to improve manufacturing product quality
- The mounting pressure on FDA to provide insight on how it intends to regulate in this space, including whether it will publish a sister document to its Action Plan for Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD),[19] focusing on drugs

Women's Health

The women's health market is predicted to be among the fastest growing investment areas within the healthcare and life sciences industry. And, FDA has increasingly focused on the criticality of representative clinical trials and women's health in drug development and approval. Congress recently capitalized on these efforts, enacting new requirements for diversity action plans for many drug clinical trials.[20] Moreover, the Supreme Court's decision in *Dobbs v. Jackson Women's Health Organization*[21] continues to reverberate, further energizing the focus on these important issues.

We'll be keeping an eye on:

- The potential FDA approval of over-the-counter birth control and other, similar over-the-counter products, as well as updated labeling of varied contraceptive products
- The continued, exponential growth of telehealth in the post-Dobbs landscape
- FDA's implementation of the new congressional mandate for increased diversity in clinical trials and the expected stakeholder development of tools, including digital health-related ones, to support recruitment and participation of women and other underrepresented groups in clinical trials

King & Spalding's FDA and Life Sciences practice is uniquely positioned to help pharmaceutical and biotechnology companies and their partners and investors understand risks and opportunities associated with product development and the FDA regulatory landscape. Please let us know if you have any questions.

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[1] Proposed Rule, *National Standards for the Licensure of Wholesale Drug Distributors and Third-Party Logistics Providers*, 87 Fed. Reg. 6708 (Feb. 4, 2022); *see also* Eva A. Temkin and Christina M. Markus, *FDA Proposes Licensing Standards for Drug Wholesalers* (Apr. 26, 2022), *available at* https://www.kslaw.com/news-and-insights/fda-proposes-licensing-standards-for-drug-wholesalers.
[2] Proposed Rule, *Nonprescription Drug Product With an Additional Condition for Nonprescription Use*, 87 Fed. Reg. 38313 (June 28, 2022); *see also* Eva A. Temkin et al., Client Alert, *A New Day (And A New Acronym) for OTC Drugs* (July 28, 2022), *available at* https://www.kslaw.com/news-and-insights/a-new-day-and-a-new-acronym-for-otc-drugs.
[3] *See e.g.*, U.S. Food & Drug Admin., GUIDANCE FOR INDUSTRY, CERTAIN OPHTHALMIC PRODUCTS: POLICY REGARDING COMPLIANCE WITH 21 CFR PART 4 (Mar. 2022); U.S. Food & Drug Admin., FDA'S OVERVIEW OF CATALYST PHARMS., INC. V. BECERRA, *available at* https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/fdas-overview-catalyst-pharms-inc-v-becerra.
[4] Inflation Reduction Act of 2022 ("IRA"), Pub. L. 117-169 (2022); *see also* David J. Farber et al., Client Alert, *Price Negotiation, Medicare Rebates, and Benefit Reform*, available at https://www.kslaw.com/news-and-insights/price-negotiation-medicare-rebates-and-benefit-reform.
[5] Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023, Pub. L. 117-180, §§ 1001-5008 (2022) (FDA User Fee Reauthorization Act of 2022).
[6] Consolidated Appropriations Act, 2023, Pub. L. 117-328, §§ 3001-3631 (2022) (Food and Drug Omnibus Reform Act of 2022 ("FDORA")).
[7] *See* Notice, *Statement of Organizations, Functions, and Delegations of Authority*, 87 Fed. Reg. 58806 (Sept. 28, 2022).
[8] *See* PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027 ("PDUFA VII Commitment Letter"), Section III.A, *available at* https://www.fda.gov/media/151712/download.
[9] *Compare United States v. California Stem Cell Treatment Center*, --- F. Supp. 3d ---, 2022 WL 3756509 (C.D. Cal. Aug. 30, 2022), *appeal pending*, No. 22-56014 (filed Oct. 28, 2022) *with United States v. U.S. Stem Cell Clinic, LLC*, 403 F. Supp. 3d 1279 (S.D. Fla. 2019), *aff'd*, 998 F.3d 1302 (11th Cir. 2021).
[10] IRA § 11002.
[11] U.S. Food & Drug Admin., GUIDANCE FOR INDUSTRY, CERTAIN OPHTHALMIC PRODUCTS: POLICY REGARDING COMPLIANCE WITH 21 CFR PART 4 (Mar. 2022).
[12] U.S. Food & Drug Admin., CLINICAL DECISION SUPPORT SOFTWARE (Sept. 2022); *see also* L. Dwyer, et al., Client Alert, *FDA's Final Clinical Decision Support Guidance: The Good News and the (Really) Bad News* (Oct. 12, 2022), *available at* https://www.kslaw.com/news-and-insights/fdas-final-clinical-decision-support-guidance-the-good-news-and-the-really-bad-news.
[13] FDORA § 3629.
[14] PDUFA VII Commitment Letter, Section IV.C.
[15] U.S. Food & Drug Admin., PROJECT FRONTRUNNER, *available at* https://www.fda.gov/about-fda/oncology-center-excellence/project-frontrunner.
[16] Executive Order 14081 of September 12, 2022, *Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy*, 87 Fed. Reg. 56849 (Sept. 15, 2022).
[17] U.S. Dep't of Health & Human Servs., FACT SHEET: HHS TAKES ACTION ON EXECUTIVE ORDER LAUNCHING A NATIONAL BIOTECHNOLOGY AND BIOMANUFACTURING INITIATIVE (Sept. 14, 2022), *available at* https://www.hhs.gov/about/news/2022/09/14/fact-sheet-hhs-takes-action-executive-order-launching-national-biotechnology-biomanufacturing-initiative.html.
[18] PDUFA VII Commitment Letter, Section I.N.5.
[19] U.S. Food & Drug Admin., ARTIFICIAL INTELLIGENCE/MACHINE LEARNING (AI/ML)-BASED SOFTWARE AS A MEDICAL DEVICE (SAMD) ACTION PLAN (Jan. 2021), *available at* https://www.fda.gov/media/145022/download.
[20] FDORA § 3601.
[21] *Dobbs v. Jackson Women's Health Org.*, 142 S.Ct. 2228 (2022).