Life Sciences Investing under Trump: Food and Drug Administration Developments

"This fast-moving regulatory landscape, combined with robust innovation in the life sciences sector, creates both opportunities and challenges for private equity sponsors."

While many other federal regulatory agencies have been marginalized or victims of regulatory paralysis, the Food and Drug Administration (FDA), under the leadership of Commissioner Scott Gottlieb, M.D., has implemented new initiatives intended to accelerate drug and device approvals and clearances, embrace innovation and new technologies, lower regulatory burdens and enhance therapeutic opportunities.

This fast-moving regulatory landscape, combined with robust innovation in the life sciences sector, creates both opportunities and challenges for private equity sponsors. As a result, the comprehensive regulatory diligence typically conducted on a potential acquisition target, or for managing exit timing or structure, needs to be accompanied by an understanding of the larger complex and multifaceted regulatory developments in the industry.

Initiatives Favorably Impacting Drug and Biologic Investment

Many of the FDA's new policies and initiatives help foster innovation and create an overall favorable environment for life sciences investing, both for companies working on innovative therapies and those producing generics and biosimilars.

- To help **accelerate the drug approval process**, the agency has established policies that support adaptive clinical trials. Adaptive trials, unlike traditional clinical trials, can be altered (in accordance with a preexisting protocol) in response to early results, allowing researchers to shift the study population or objectives, for example. A single adaptive trial could replace multiple lengthy and expensive trials and could lead to a shorter, less expensive approval process. In addition to adaptive trials, Gottlieb has also emphasized **the use of computation modeling** in a potential effort to abandon or modify the typical three stages of clinical trials.
- The FDA has placed a priority on **using real-world data and real-world evidence** to support its decision making. The FDA currently uses real-world data to monitor post-market safety and adverse events and to make

Continued on page 2

Private Equity Report
Spring 2018
Volume 18, Number 1

regulatory decisions. The 21st Century Cures Act requires the agency to go further and to develop a regulatory framework and guidance on how real-world evidence can be used to support approval of new indications for approved drugs or to support or satisfy post-approval study requirements.

or conditions and, by the end of the year, had eliminated the entire backlog of pending orphan drug designation requests and **approved a record number of drugs with orphan indications**. In addition, the promise of targeted therapies, which may be extremely effective for certain subpopulations but not for others, has prompted the FDA to issue guidance on developing clinical trials for targeted therapies for small numbers of patients and on the diagnostic devices used alongside these therapies to identify patients eligible for treatment.

"In what would be a significant deregulatory move, the FDA is planning to propose regulations this year that will increase access to prescription drugs by allowing them to be sold over-the-counter with added safeguards."

- Last year, the FDA issued its first three **approvals for gene therapy drugs**—part of a larger wave of immunotherapies that could one day lead to cancer vaccines and other breakthroughs. Currently there are hundreds of such gene- and cell-based treatments in clinical trials. To support the development of these therapies, the FDA has established a comprehensive policy framework as well as a **pathway for qualifying regenerative medicine therapies** to receive the FDA's fast track and breakthrough designations.
- The FDA announced its "Orphan Drug Modernization Plan" in June 2017 for treatments of rare diseases
- In what would be a significant deregulatory move, the FDA is planning to propose regulations this year that will **increase access to prescription drugs by allowing them to be sold over the counter** with added safeguards. The FDA intends to promote innovative approaches to ensure that customers can self-select appropriate drugs on their own.

Initiatives Favorably Impacting Medical Device, Digital Health and Diagnostics Investment

As with drugs and biologics, the agency is actively working to promote innovation and first-in-class products in the realm of devices and diagnostics.

- To lessen the uncertainty in the device approval and clearance processes, the FDA issued final guidance **updating policy guidelines on the types of device modifications that require a new 510(k)** instead of mere documentation by the manufacturer. In addition, for the first time in well over a decade, the FDA **updated two "least burdensome" guidance documents** that implement the Congressional directive to eliminate unnecessary burdens that may delay the marketing of beneficial new products.
- The FDA announced plans to issue draft guidance that would **allow manufacturers to demonstrate substantial equivalence**, and obtain device clearance, using objective safety and performance criteria rather than having to compare a new device with specific predicate devices that may be decades old and difficult to obtain. Further, the FDA plans on issuing draft guidance in early 2018 that will place **increased focus on post-market**

Continued on page 3

Private Equity Report
Spring 2018
Volume 18, Number 1

follow-up studies to accelerate the market entry of medical devices and facilitate patient access to innovative products. The agency is also **reorganizing the Center for Devices and Radiological Health** by combining several of its review, compliance and surveillance functions into a single unit, the Office of Product Evaluation and Quality. The FDA expects this reorganization to increase the efficiency of the Center's activities, including application review.

"The agency is also reorganizing the Center for Devices and Radiological Health by combining several of its review, compliance and surveillance functions into a single unit, the Office of Product Evaluation and Quality."

- The FDA is in the process of **issuing new draft and final guidance documents related to medical software**, including guidance clarifying which categories of medical software functions and digital health technologies are subject to the FDA's jurisdiction and when to submit a 510(k) for a software change to an existing device. Areas that fall outside the FDA's jurisdiction—such as software meant for administrative support, patient decision support and electronic patient records, and to help maintain or encourage a healthy lifestyle—will face a lower regulatory burden and thus may be particularly attractive for new development. The FDA has also recently introduced the **Software Precertification (Pre-Cert) Pilot Program**, through which the FDA may pre-certify certain companies based on their quality systems and allow for a lower bar for any new digital health products distributed by these companies. We expect the FDA to continue to focus its regulatory efforts on high-risk products, while loosening the regulatory burdens on lower-risk digital health products, consistent with the mandates of the 21st Century Cures Act.
- Responding to what it calls a "new era of 3D printing of medical products," the FDA has issued guidance addressing technical considerations for manufacturers. The FDA also is in the process of **developing a regulatory framework for manufacturers of 3D-printed personalized devices**, but the guidance could result in higher regulatory burdens—including decreased flexibility and higher costs—for non-traditional manufacturers such as university hospitals that are already manufacturing 3D-printed devices for individual patients. As the FDA develops the regulatory framework, interested sponsors should pay close attention in order to take advantage of opportunities and avoid regulatory pitfalls.
- Companies offering certain types of **direct-to-consumer genetic tests** had several regulatory burdens reduced in November 2017. First, the FDA issued an order **exempting genetic carrier screening tests from premarket review**. This was followed by notice of the agency's intent to allow "genetic health risk assessment" (*i.e.*, predictive) tests to be exempted from premarket review under certain conditions. If finalized, manufacturers would only need a one-time review to ensure that they meet FDA requirements, after which they may market new tests without further review. In addition, in March 2018, the FDA approved for the first time a direct-to-consumer genetic test (using saliva) to test for three genetic mutations associated with breast cancer in people of Ashkenazi (Eastern European) Jewish descent.

Continued on page 4

- The debate continues around the regulation of **laboratory-developed tests** (LDTs)—in vitro diagnostic tests that are designed, manufactured and used within a single laboratory such as a hospital's in-house laboratory. The device industry is pitted against the clinical labs that develop and market diagnostics in the absence of FDA oversight (but subject to other Federal and state regulatory requirements). Commissioner Gottlieb is looking to Congress to establish the FDA's regulatory role in these products. In the meantime, the FDA is **encouraging LDTs to seek voluntary approval** and is pursuing ways to make the approval or 510(k) clearance process less burdensome. As one example, the FDA accredited the New York State Department of Health as an FDA third-party reviewer of in vitro diagnostics.

FDA Regulatory Initiatives with More Nuanced Implications for Life Sciences Investing

The implications of several FDA initiatives will depend on where the company sits in the market. Here we discuss four such areas: generic drugs, biosimilars, opioids and drug compounding.

- Regulations impacting generic drugs are of interest because the competition that generics introduce affects **drug pricing**. Commissioner Gottlieb has repeatedly expressed frustration with innovator companies that allegedly attempt to delay the entry of generic drugs into the market through two tactics: slowing down negotiations with generic drug companies over the use of the post-market risk management plans that innovators and generics are required to share for some drugs, and limiting generic company access to innovator drugs in order to perform the bioequivalence studies necessary for generic approval. In response, the FDA recently issued a guidance document **reducing the paperwork necessary for a shared Risk Evaluation and Mitigation Strategies (REMS) system**, and the agency is also expected to release guidance addressing generic drug company access to innovator drugs.
- The FDA **expanded the number of ways generic drug applicants can qualify for priority review** of their Abbreviated New Drug Application and issued multiple guidance documents intended to increase the efficiency of generic application review. The agency has also implemented strategies to **better publicize approved innovator drugs that are off-patent and off-exclusivity** and is working with the U.S. Pharmacopeial Convention (USP) to develop standards for those drugs.
- In 2017, the FDA **approved five biosimilars**, and Commissioner Gottlieb believes that biosimilar development, and resulting FDA approvals, is poised to significantly increase in the near future. He indicated that the agency will be releasing a **Biosimilar Innovation Plan** during 2018 that is intended to encourage biologics competition.
- The FDA is responding to the opioid crisis by increasing **heightened regulatory scrutiny of opioid products and their manufacturers**. It removed Endo Pharmaceuticals' Opana ER from the market and may take similar action against other products where it believes benefits no longer outweigh risks. The FDA is developing changes for immediate-release opioid labeling, requesting packaging changes to limit abuse, considering including the potential for abuse in the approval process for new opioid products and implementing more stringent post-approval obligations.
- At the same time, the agency is **encouraging innovations to treat opioid addiction** and the development of abuse-deterrent generic formulations of opioid products already on the market. The FDA has approved multiple therapies to treat opioid addiction, including a drug-device combination product (monthly

Continued on page 5

Private Equity Report
Spring 2018
Volume 18, Number 1

buprenorphine injections) and a neurostimulator device developed by Innovative Health Solutions, Inc.

- The FDA has indicated that it aims to strengthen its **oversight over compounding pharmacies and outsourcing facilities** and intends to enforce higher quality standards. Since the 2012 meningitis outbreak that focused attention on the issue, the agency has conducted more than 425 inspections of compounding pharmacies and outsourcing facilities, during which it observed "problematic conditions during the vast majority of these inspections," and has overseen more than 140 recalls of compounded drugs. Notably, a **private equity fund was recently named in a Department of Justice lawsuit** targeting a compounding pharmacy for violations of the False Claims Act.

Private equity sponsors investing in the life sciences sector should be encouraged by the direction the FDA is currently taking. However, understanding the nuanced ramifications of the many new FDA initiatives is critical to making thoughtful and forward-looking investments in this industry. And it is equally important that private equity sponsors ensure that any FDA-regulated company has a sophisticated regulatory infrastructure in place to address compliance on an ongoing basis.

"Private equity sponsors investing in the life sciences sector should be encouraged by the direction the FDA is currently taking."

To read the complete guide, visit https://www.debevoise.com/~/media/files/insights/publications/2018/03/20180315_private_equity_guide_to_life_sciences_investing_under_the_trump_administration.pdf.

Andrew L. Bab
albab@debevoise.com

Jennifer L. Chu
jlchu@debevoise.com

Kevin Rinker
karinker@debevoise.com

Paul D. Rubin
pdrubin@debevoise.com

Melissa B. Runsten
mrunsten@debevoise.com