SPECIALTY PHARMA

Strategies For Business Development

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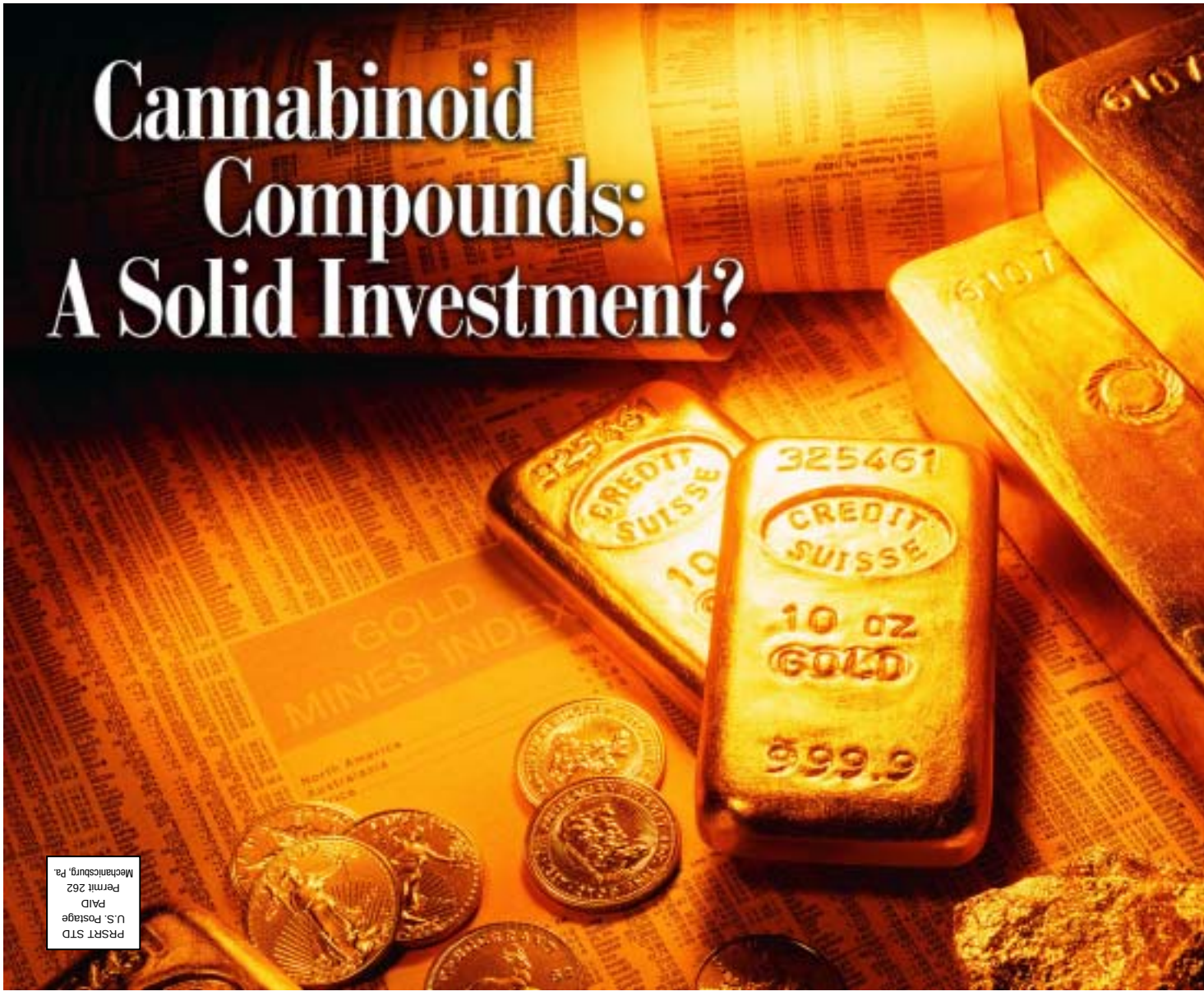

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James N. Czaban is a Shareholder in the Washington, DC, office of Heller Ehrman White & McAuliffe, where he leads the FDA Practice Group. Jim has more than 12 years experience in FDA regulatory and legal matters, and represents both specialty and large pharmaceutical and biotechnology companies in matters involving the regulation of drugs and biologics. His work encompasses all stages of a product's lifecycle, including pre-clinical research, development of appropriate clinical stage regulatory strategies (including the effective use of meetings with FDA), drafting and negotiation of marketing applications (NDAs, 505(b)(2) NDAs, BLAs, ANDAs, Rx to OTC switches), post-approval promotional compliance (DDMAC advertising oversight, Medicare/Medicaid reimbursement, fraud, abuse, and anti-kickback), and Hatch-Waxman/lifecycle management issues. He also regularly advises clients on licensing agreements (for products and patents), mergers, acquisitions, and other business transactions involving FDA-regulated products and entities, and frequently represents clients in contested administrative proceedings (Citizen Petitions and private negotiations with FDA), as well as FDA-related lawsuits arising under the Administrative Procedure Act and the patent laws. Jim has contributed to three legal treatises, written numerous articles, and lectured extensively at law school and industry courses on Food & Drug law. He has also been named one of Washington DC's "Top Lawyers" in Food & Drug Law by *Washingtonian Magazine*.

Challenges & Strategic Opportunities in the Highly Regulated World of Specialty Pharma

By: James N. Czaban, Esq., Shareholder, Heller Ehrman White & McAuliffe LLP

Introduction

The Specialty Pharma sector is different than the familiar large pharmaceutical business model, but the industry is difficult to precisely define because the differences are manifested in a variety of ways by different specialty companies. Some Specialty Pharma companies focus on particular disease states or therapeutic drug classes, while some focus on proprietary drug delivery or formulation technology that can be applied to molecules across multiple clinical areas. Others use a market-based approach, focusing on promising drugs that Big Pharma companies have chosen not to develop. Still, others seek to market improved variations of existing drugs, often using the 505(b)(2) NDA approach to FDA approval.

The reasons for, and benefits of, particular Specialty Pharma business models also vary. Some early-stage companies see a niche focus as a stepping stone to future expansion, while others may have narrowed their focus from a former broad-based model due to financial or other business reasons. Others have found their niche due to particular individual interests of the company founders or due to the unique technological know-how and intellectual property rights of the company. The one unifying fact of life for Specialty Pharma companies of all varieties is the complex FDA regulatory scheme that governs the development, approval, and marketing of new drug products. This scheme presents difficult and unpredictable obstacles to approval, but also offers valuable market opportunities for companies willing to invest in a well-planned legal/regulatory strategy.

Life-Cycle Management Strategies For Unpatented New Drugs

For Specialty Pharma companies, life-cycle management (LCM) is of crucial importance, but this is especially true for products with limited patent protection. Absent a patent covering the active pharmaceutical ingredient of a product, companies must rely on a combination of formulation and method-of-use patents, as well as the various regulatory exclusivities available under the Federal Food, Drug, and Cosmetic Act. These exclusivities include the 5-year New Chemical Entity (NCE) exclusivity, 3-year new product or new use exclusivities, pediatric extensions, and Orphan Drug Exclusivity, where applicable. Savvy companies also plan well in advance for strategic product improvements and line extensions that can extend the revenue stream for underpatented products, sometimes for years. More recently, when all traditional LCM strategies have been exhausted, some innovator companies have turned the controversial strategy of licensing "authorized generics" on the eve of true generic competition, in the hope of wringing additional profits in the multi-source phase of a product's life cycle.

LCM strategies can be complex, drug-specific, and difficult to implement and must be planned for well in advance (even before initial approval) if they are to be effective. Moreover, in August 2003, the FDA implemented new regulations governing the role of patents in the new and generic drug approval scheme. And in December 2003, Congress enacted important changes to the Hatch-Waxman amendments as part of the Medicare Reform Act (MMA) that are designed to eliminate obstacles to generic drug approval. The changes brought about by the MMA are complex and contain ambiguities that are yet to be interpreted and implemented by the FDA.

The Ins & Outs of 505(B)(2) NDAS

The FDA permits approval of drugs, and potentially certain biologic products, under a controversial hybrid statutory approval mechanism known as a 505(b)(2) NDA. A 505(b)(2) NDA is a combination of a full NDA and a generic ANDA that allows a simplified application process for variations of previously approved drugs in which the new modified product is not eligible for the traditional generic ANDA process. The 505(b)(2) NDA takes advantage of publicly available safety and efficacy data, and the FDA's prior approval of similar products, as a means to avoid at least some of the costly and time consuming clinical and preclinical studies on eligible drugs. Some Specialty Pharma companies focus almost exclusively on 505(b)(2)-eligible drugs, but because this pathway can cut years of effort and millions of dollars from development budgets, use of 505(b)(2) NDAs should be of interest to all Specialty Pharma companies.

Preparing & Conducting Persuasive Meetings With The FDA

Since passage of the *FDA Modernization Act of 1997* (FDAMA), formalized meetings between the FDA and drug sponsors at various stages of product development (pre-IND, pre-NDA) have become routine, but companies that treat these meetings as routine can fail to reap the advantages possible with a well-developed meeting strategy, or worse, fall into costly and time-consuming traps that could have been avoided with appropriate preparation and follow-up. The FDA's approach and follow-up to pre-IND and pre-NDA meetings is steeped in regulatory complexities and nuances that can easily be misinterpreted by inexperienced or unprepared sponsors, with costly results.

Maximizing Marketing Impact Without Running Afoul Of Government Regulators

Once a drug is approved, the FDA's role in regulating the product is far from over. The FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC) monitors prescription drug advertising and promotional activities and enforces the often obscure and counterintuitive promotional rules for these products. "Off-label" promotion is one area of particular interest to pharmaceutical companies, and of particular concern to the FDA. Yet, there are ways to make off-label information available to prescribers in ways that do not run afoul of the FDA's restrictive promotional regulations and policies.

DDMAC is not the only governmental agency monitoring drug promotion. The Office of the Inspector General (OIG) of the Department of Health and Human Services (HHS) regulates and enforces the anti-kickback and fraud and abuse provisions of the Medicare and Medicaid laws, and both the OIG and state Attorneys General have brought high profile civil and criminal actions against drug companies and individual employees for violations of these rules.

Patent Strategies For Specialty Pharmaceuticals

Patenting strategies for pharmaceutical products and technologies have evolved in increasingly complex ways in recent years, partly in response to regulatory (life-cycle management) pressures, and partly due to the increasingly competitive landscape for companies seeking venture or public financing, or merger opportunities. Maximizing the value of patenting strategies is a crucial aspect of any Specialty Pharma business plan.

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Licensing, Co-Development & Co-Marketing Strategies For Specialty Pharmaceuticals

Licensing intellectual property, drug candidates, and approved marketed products is an essential business tool for Specialty Pharma companies, and effectively drafting and negotiating such licenses can make a major difference in the ultimate value of the deal. Licensing issues are of interest to Specialty Pharma for several reasons. Some companies rely on in-licensed products to quickly establish a portfolio of approved or late-stage drug candidates without conducting the arduous drug discovery and development work that can take decades and cost hundreds of millions of dollars, with no guarantee of an approvable drug. Other companies focus on the early discovery and development work and rely upon out-licensing to larger companies to take the drug through the more cumbersome Phase III trials and, hopefully, across the finish line to FDA approval.

Co-development agreements offer a hybrid version of one-way licenses and co-marketing deals offer opportunities for smaller specialty drug companies, or even larger foreign manufacturers, to build US market recognition as a full-fledged research and marketing company. Using the expertise and resources of larger or more experienced companies can maximize physician awareness and market penetration in the increasingly crowded pharmaceuticals market.

Author's Note

The preceding discussed some of the legal and regulatory issues facing Specialty Pharma companies. Future columns will discuss these and other issues in greater detail. This column is intended to be interactive. Reader comments, questions, and suggestions for future column topics are welcome and encouraged. The author can be reached at (202) 912-2720, or by e-mail at jczaban@hewm.com.