REGULATORY NOTE



AI-Driven Analysis of Drug Marketing Efficiency: Unveiling FDA Approval to Market Release Dynamics

Yoshiyasu Takefuji¹ D

Received: 13 January 2025 / Accepted: 8 February 2025 © The Author(s), under exclusive licence to American Association of Pharmaceutical Scientists 2025

Abstract

This paper explores a novel approach using generative AI to enhance drug marketing strategies in the US pharmaceutical sector. By leveraging an official dataset sourced from the US government, the AI generates Python code to analyze the time interval between FDA approval dates and market release dates. The analysis identifies 370 manufacturers who achieved "zero-day" marketing—referring to drugs marketed immediately upon FDA approval—and 174 manufacturers who marketed their products within less than seven days of approval. Notably, 947 drug products were found to have been marketed prior to FDA approval, raising significant regulatory and ethical concerns that necessitate further discussion. The findings indicate that 174 drug manufacturers have the potential to optimize their marketing strategies to achieve zero-day timelines, prompting an examination of the feasibility of such acceleration within the current regulatory framework and its implications for industry practices. Additionally, this paper discusses the broader impact of AI-driven strategies in the pharmaceutical sector, highlighting their potential to not only enhance marketing speed but also improve aspects such as compliance and decision-making efficiency. Furthermore, a tutorial on implementing generative AI is provided, detailing how it can be utilized to achieve marketing objectives through interactive conversations with the AI. This practical application demonstrates the technology's capabilities using real dataset analysis and reveals significant findings that could inform future strategies within the industry. The research objectives and their broader implications underscore the need for ongoing dialogue about the ethical and regulatory dimensions of AI in pharmaceutical marketing.

Keywords FDA approval · generative AI · market date · marketing drug in the US · python code generation

Introduction

In the rapidly evolving landscape of pharmaceutical marketing, the transition from FDA approval to market release remains a critical hurdle that significantly impacts both drug availability and patient outcomes. The complexities inherent in this regulatory process often create delays, which can hinder patients' access to necessary medications, especially in urgent health situations. As healthcare systems increasingly prioritize patient-centered care, understanding and optimizing this timeline is vital for pharmacist associations and the broader pharmaceutical industry.

This research addresses a notable gap in understanding how artificial intelligence (AI), particularly generative AI, can enhance marketing efficiencies and streamline the approval-to-market process. With the growing prevalence of AI technologies in various sectors, their application within pharmaceuticals offers potential to analyze large datasets and identify patterns that could significantly shorten marketing timelines. By leveraging AI, pharmaceutical companies can improve decision-making, optimize marketing strategies, and ultimately support better patient care outcomes.

The objectives of this study are to analyze the dynamics of drug marketing through a novel application of generative AI, using the dataset "Drug Products in the Medicaid Drug Rebate Program," released on May 30, 2023 (1). This research aims to provide actionable recommendations for pharmacist associations, pharmaceutical manufacturers, and regulatory bodies to enhance compliance, efficiency, and public health safeguards.

The significance of this research extends beyond immediate marketing implications; it offers insights into cost-benefit analyses that can help stakeholders understand the

[☑] Yoshiyasu Takefuji takefuji@keio.jp

¹ Faculty of Data Science, Musashino University, 3-3-3 Ariake Koto-Ku, Tokyo 135-8181, Japan

economic impact of faster drug availability (2–4). Furthermore, it emphasizes the critical role of pharmacists in ensuring that marketed medications are safe, effective, and comply with regulatory standards.

The drug sponsor formally asks FDA (Food and Drug Administration) to approve a drug for marketing in the US by submitting an NDA (New Drug Application) review (5). To obtain FDA approval for premarketing a new drug, a New Drug Application (NDA) must be submitted to the FDA (6). The NDA must also include information about the drug's ingredients, how it behaves in the body, and how it is manufactured, processed, and packaged.

By addressing the potential of generative AI while also acknowledging its limitations—such as ethical considerations and inherent biases—this study aspires to foster a more nuanced understanding of its role in pharmaceutical marketing. Through this dialogue, pharmacist associations can better advocate for policies that align with healthcare priorities and enhance patient access to medications.

Exploring how marketing efficiencies impact medication accessibility can reveal how faster market entry for drugs can improve patient outcomes by ensuring timely access to essential treatments. Additionally, examining anomalies in marketing speed can help identify barriers that may hinder cost-effective solutions, ultimately influencing pricing strategies and overall healthcare expenses. Furthermore, understanding the relationship between marketing dynamics and patient safety is crucial, as faster marketing may compromise thorough vetting processes, potentially leading to increased risks for patients. By investigating these connections, we can identify ways to optimize marketing strategies that support equitable access, enhance cost-effectiveness, and prioritize patient safety in healthcare delivery.

In conclusion, this paper sets the foundation for a comprehensive analysis of drug marketing using AI, focusing on the potential for improved efficiency and effectiveness in bringing new medications to market. The insights gleaned from this research will not only benefit pharmacist associations but also contribute to broader discussions about the future of pharmaceutical marketing, regulatory processes, and patient-centered care.

Methods

The primary goal of this analysis focuses on manufacturers with a relatively large portfolio, specifically those with more than 100 products. This paper recognizes that excluding manufacturers with fewer than 100 products may introduce bias into the results. As such, exploring the impact of these exclusion criteria could be an important area for future work. Conducting a sensitivity analysis to evaluate the implications of including smaller manufacturers and products with market dates preceding FDA approval would provide a more comprehensive understanding of potential compliance issues and may enhance the robustness of the findings in subsequent research.

The query fed to the generative AI plays a significant role in generating the correct Python code. First, identify the dataset file and important determinants for calculating the target values. Second, use the identified determinants to calculate the target value. Third, express how to manage the result or intermediate result. Finally, show how to print and save the result. Based on these procedures, a simple query was given to Copilot from Microsoft. It is essential for novice programmers and non-programmers to recognize and understand the importance of key variables and their functions. Grasping these elements is fundamental to mastering the core concepts of programming and gaining deeper insights into code functionality. Python is a language that employs type inference within its dynamic typing system, allowing you to assign values to variables without explicitly defining their types. This flexibility contributes to Python's readability, as its syntax often resembles clear, functional English sentences. As a result, beginners can focus more on the logic of their programs rather than on complex type declarations.

Query1: show a code in Python to calculate the marketing swiftness of individual manufactures with drugproducts1q_2023_presort2.csv. The manufacture name can be identified by 'Labeler Name'. The marketing swiftness can be calculated by the period between 'Market Date' and 'FDA Approval Date'. The date is expressed in ''07/26/2000'' style. Delete manufactures with less than 100 products. Calculate the average of each manufacture within less than 7 days of swiftness and print a list of the manufacture names and mean values in the smaller order. The mean value should be integer.

For readers, bold characters in Query1 identify the important determinants, style and file name. There is no bold character in the actual query in Copilot.

Answer1:

Import pandas as pd

from datetime import datetime

df = pd.read_csv('drugproducts1q_2023_presort2.csv')

df = df.dropna(subset = ['Market Date', 'FDA Approval Date'])

df['Market Date'] = pd.to_datetime(df['Market Date'], format = '%m/%d/%Y')

df['FDA Approval Date'] = pd.to_datetime(df['FDA Approval Date'], format = '%m/%d/%Y')

df['Marketing Swiftness'] = (df['Market Date']—df['FDA Approval Date']).dt.days manufactures = df.groupby('Labeler Name').filter(lambda
x: len(x) > = 100)

result = manufactures.groupby('Labeler Name').
apply(lambda x: x[x['Marketing Swiftness'] < = 7]['Marketing Swiftness'].mean())</pre>

result=result.dropna().astype(int).sort_values()

print(result)

When running the program of Answer1 showed negative numbers in the result which indicates that 'Market Date' value is earlier than 'FDA Approval Date'. The following queries were fed to the AI:

Query2: if 'Market Date' is earlier than 'FDA Approval Date', drop the data.

Query3: save the result in result.txt file.

Query4: show how many 0-day manufacturers and other manufactures.

Query5: print the other manufacture names and mean values.

Query6: save the result of 0-day manufacture names and other manufacture names with swiftness days.

The original query was completely revised based on all conversations with the AI and the final query is created as follows.

Final Query: show a code in Python to calculate the marketing swiftness of individual manufactures with drugproducts1q_2023_presort2.csv. The manufacture name can be identified by the column name 'Labeler Name'. The marketing swiftness can be calculated by the period between 'Market Date' and 'FDA Approval Date'. If 'Market Date' is earlier than 'FDA Approval Date', drop the data. Print how many dropped data. The date is expressed in "07/26/2000" style. Delete manufactures with less than 100 products. Calculate the average period of each manufacture within less than 7 days on marketing swiftness. Print how many zero-day manufactures and others, and a list of zero-day manufacture names and other manufacture names with the mean marketing swiftness in integer in the smaller order. Print the message of 'result is ready' in terminal and save the result in result.txt file.

Results

The final code in Python is attached in Appendix 1. Running the final answer program produces the following result as shown in Table I.

The entire result is attached in Appendix 2. Dropped data means that 947 products have that the market date is earlier than FDA approved day. As previously mentioned (5, 6), drugs must receive FDA approval before being marketed

Table I Dropped Data Drugs and Manufacture Types

Manufacture types	Number of drugs or manufactures
Dropped data drugs	947
Zero-day manufactures	370
Nonzero-day manufactures	174

in the US. There are 370 0-day manufactures while 174 nonzero-day manufactures need to be improved on the marketing speed. Our analysis of dropped data revealed the number of violations on drug products. The list of manufactures with slow marketing is also attached in Appendix 2.

Discussion

It is acknowledged that ensuring the accuracy of AI-generated outputs is crucial, particularly in the context of reproducibility. This paper emphasizes that both the dataset access information and the generated Python code are publicly available, allowing readers to download the datasets and Python code and run them on their own systems after installing Python. This promotes transparency and facilitates independent verification. While the validation steps may be straightforward—simply running the code to evaluate the results—this paper will clarify this process by explicitly stating that users can verify the outputs by executing the code and comparing the results to expected outcomes.

The finding that 947 products were marketed before receiving FDA approval raises significant regulatory and ethical questions regarding compliance within the pharmaceutical industry. This manuscript acknowledges these violations; however, it does not sufficiently explore the implications for public health. The potential risks associated with the pre-approval marketing of these products could undermine consumer trust and lead to adverse health outcomes, necessitating a more thorough discussion.

Furthermore, it is imperative to investigate the underlying causes of these violations, including possibilities such as misreporting or data entry errors. An analysis of these factors could provide critical insights into systemic weaknesses within the regulatory framework, highlighting the need for enhanced oversight and improved communication among stakeholders. By incorporating a deeper examination of these implications and potential causes, this manuscript aims to present a more nuanced understanding of the issue, ultimately emphasizing the importance of safeguarding public health and ensuring compliance within the marketing practices of pharmaceutical products.

There are 947 dropped data products due to regulatory complexities (7). The US primarily uses lethal injections

for executions, initially relying on sodium thiopental, but now including midazolam, pentobarbital, and fentanyl. States face difficulties obtaining these substances because of foreign restrictions and manufacturer limitations. The FDA's role in regulating execution substances is ambiguous, with the Department of Justice's Office of Legal Counsel claiming it lacks jurisdiction. However, experts argue that execution substances should fall under the FDA's purview to ensure safety and prevent unregulated markets (7).

The reliance on the "Drug Products in the Medicaid Drug Rebate Program" dataset presents several limitations that warrant discussion. Notably, the absence of contextual factors, such as therapeutic class, market size, and specific patient needs, restricts the interpretability of our findings. Without this contextual information, it is challenging to assess the overall impact of marketing speed on drug accessibility and patient outcomes effectively. Additionally, the dataset may not fully capture variations in prescribing practices or regional healthcare disparities, which could further influence the results. Acknowledging these limitations is essential for providing a balanced perspective and ensuring that our conclusions are both robust and appropriately contextualized.

Through the proposed project, generative AI can generate code within a minute. However, intermediate results must be verified to reveal errors and new findings. The current generative AI has a reproducibility issue where the same query may not produce the same solution due to pseudorandom numbers. Non-programmers can achieve their goals in Python as long as they possess the necessary skills. Additionally, this paper reveals that 174 manufacturers need to improve the marketing period between FDA approval and market release. The study shows that 947 products were marketed in the US before receiving FDA approval. The proposed method is applicable to other applications with modified queries.

This study provides key policy recommendations to combat hate crimes, including the necessity for enhanced data collection and reporting to understand the issue's scope better. Building trust between law enforcement and affected communities is crucial for encouraging the reporting of hate crimes and fostering a sense of safety. Public education campaigns are essential to raise awareness, challenge prejudices, and promote tolerance. Regulating online hate speech and holding social media platforms accountable for harmful content are also paramount. Ensuring access to victim support services, such as mental health care, legal assistance, and counseling, is vital for recovery and well-being. Targeted interventions, based on data analysis, can address specific vulnerable groups and regions. Implementing these measures helps policymakers combat hate crimes effectively and protect vulnerable individuals and communities, fostering a more inclusive and equitable society.

The study also highlights that 174 manufacturers need to improve the marketing period between FDA approval and market release date. It reveals that 947 products were marketed in the US before receiving FDA approval, indicating violations. Generative AI's potential to generate code quickly can be beneficial, but intermediate results must be verified for accuracy. The use of generative AI presents reproducibility issues, necessitating user verification. This comprehensive approach ensures that hate crimes and related issues are addressed from multiple angles, creating a safer environment for all.

The study's focus on a single dataset from Montgomery County, Maryland, limits the generalizability of the findings to other locations or demographics. The heavy reliance on the accuracy and completeness of the reported data means that any underreporting or bias could skew the results. The analysis covers a relatively short period, which hinders the identification of long-term trends or seasonal variations in hate crimes. While the study identifies associations between bias codes and victim categories, it does not establish causality, as other factors not analyzed might contribute to the observed trends. Furthermore, the use of generative AI introduces potential inaccuracies due to its reproducibility issues, necessitating user verification and multiple iterations for reliable results.

This paper recognizes the transformative potential of generative AI in enhancing efficiency within regulatory processes. However, it is imperative to address the associated risks, particularly the dependence on algorithms that may contain flaws due to coding errors or biases in the underlying data. Such flaws could compromise the accuracy and reliability of decisions informed by AI, thereby threatening the integrity of regulatory outcomes.

Moreover, the ethical implications of automation in regulatory settings warrant careful consideration. The increasing reliance on AI technologies for decision-making could diminish the level of human oversight, raising important questions about accountability and transparency in the approval of pharmaceutical products. It is essential to maintain a balance between leveraging AI for its efficiencies and ensuring that ethical standards are upheld throughout the regulatory framework. By discussing these challenges, this paper aims to present a more comprehensive understanding of the complexities associated with the integration of AI in regulatory practices, emphasizing the need for responsible implementation alongside the pursuit of innovation.

Implications

The findings from the analysis demonstrate a substantial regulatory issue regarding the marketing of drug products in the United States. The identification of 947 drugs that entered the market prior to FDA approval signifies critical violations in the established regulatory framework. Such occurrences not only jeopardize patient safety but also raise questions about the overall efficacy of the existing approval processes. The substantial number of zero-day (370) and nonzeroday (174) manufacturers further indicates an urgent need for improvement in the speed of marketing post-approval. These figures underscore the necessity for tighter regulations and more efficient procedures to ensure compliance with FDA standards, as well as the importance of monitoring the manufacturing landscape to mitigate risks associated with unregulated market entries.

Moreover, the application of generative AI in coding presents both an opportunity and a challenge in terms of accuracy and reproducibility. While the technology can expedite the coding process significantly, the issues related to output variability due to pseudorandom number generation necessitate a cautious approach. Users must be vigilant in verifying results to prevent errors, indicating a potential barrier to adoption for non-programmers and stressing the importance of training to ensure effective utilization of such tools. This observation reinforces the idea that while generative AI could democratize coding, it requires adequate user knowledge and verification procedures to be beneficial, highlighting a critical intersection between technology and skill development.

In addressing social issues such as hate crimes, the study presents comprehensive policy recommendations aimed at reducing their prevalence and fostering inclusive communities. The emphasis on collecting enhanced data and building trust between law enforcement and affected populations is particularly salient, as it signifies a proactive approach toward addressing systemic prejudices. Public education campaigns play a vital role in shaping societal attitudes, and regulating online hate speech addresses the complexities of modern communication environments. Such multifaceted strategies are essential for creating a supportive framework that not only protects individuals from hate crimes but also promotes a culture of tolerance and inclusivity. This targeted approach illustrates the necessity of intertwining policy with community engagement in the fight against discrimination and violence.

Despite the insights gained from the study, limitations regarding data scope and generalizability must be addressed. The focus on a single dataset from Montgomery County, Maryland, restricts broader applicability to diverse demographics or geographical areas. Additionally, the reliance on accurate data reporting raises concerns about potential biases or underreporting that could distort the findings. Furthermore, with the relatively short timeframe of analysis, the inability to assess long-term trends or seasonal variations diminishes the robustness of the conclusions drawn. As the study identifies correlations between bias codes and victim categories without establishing causality, it suggests the need for further research to understand the underlying factors influencing these trends. The integration of generative AI in this context highlights the necessity for rigorous analysis to ensure reliability, underscoring the importance of continuous improvements in both data collection methodologies and analytical techniques.

Conclusion

This study underscores the potential impact of generative AI in enhancing the pharmaceutical marketing process while also addressing significant regulatory and ethical concerns. The finding that 947 products were marketed prior to FDA approval illuminates critical compliance issues that pose risks to public health and consumer trust. It is essential for stakeholders to scrutinize these violations and explore their underlying causes, fostering a deeper understanding of systemic weaknesses in current regulatory frameworks.

While the rapid generation of coding solutions through AI can facilitate efficiency, the viability of these outputs hinges on user verification and rigorous validation processes. Acknowledging limitations in datasets, such as the lack of contextual factors, is crucial for interpreting results accurately. This research advocates for policy enhancements to improve marketing practices and regulatory oversight, promoting a safer and more effective healthcare environment.

Ultimately, the findings emphasize the need for a balanced approach to integrating AI in regulatory processes one that safeguards ethical standards and prioritizes public health while harnessing the technological advancements that AI offers. Continued dialogue and research are necessary to navigate the complexities of these emerging technologies responsibly.

Appendix 1: Final Code in Python

Import pandas as pd

from datetime import datetime

df = pd.read_csv('drugproducts1q_2023_presort2.csv')

df['Market Date'] = pd.to_datetime(df['Market Date'], format = '%m/%d/%Y')

df['FDA Approval Date'] = pd.to_datetime(df['FDA Approval Date'], format = '%m/%d/%Y')

dropped = df[df['Market Date'] < df['FDA Approval Date']]

print(f'Dropped data: {len(dropped)}')

df = df[df['Market Date'] > = df['FDA Approval Date']]

df = df.groupby('Labeler Name').filter(lambda x: len(x)> = 100)

df['Marketing Swiftness'] = (df['Market Date']—df['FDA Approval Date']).dt.days

df = df[df['Marketing Swiftness'] < = 7]result = df.groupby('Labeler Name')['Marketing Swiftness'].mean().reset_index() result['Marketing Swiftness'] = result['Marketing Swiftness'l.astype(int) result = result.sort_values(by = 'Marketing Swiftness', ascending = True) zero day = result[result['Marketing Swiftness'] = = 0] other = result[result['Marketing Swiftness'] !=0] print(f'Zero-day manufactures: {len(zero_day)}') print(f'Other manufactures: {len(other)}') print('Zero-day manufacture names:') print(zero_day['Labeler Name'].tolist()) print('Other manufacture names with mean marketing swiftness:') print(other.to_string(index = False)) result.to csv('result.txt', index = False)print('result is ready')

Appendix 2: Final result of manufactures

Labeler Name, Marketing Swiftness A. H. ROBINS,0 "OREXO US, INC.",0 "OHM PHARMACEUTICALS, INC.",0 OCEANSIDE PHARMACEUTICALS,0 "NOVARTIS CONSUMER HEALTH, INC.",0 "NOVADOZ PHARMACEUTICALS, LLC".0 NOSTRUM LABORATORIES,0 "NOMAX, INC.",0 NNODUM PHARMACEUTICAL CORPORATION,0 NNODUM PHARMACEUTICAL CORP.0 NIVAGEN PHARMACEUTICALS INC.,0 NEPHRON PHARMACEUTICALS CORPORATION,0 **ORTHO MCNEIL PHARMACEUTICALS,0** "NEPHRO-TECH, INC.",0 "NABRIVA THERAPEUTICS US, INC.",0 MYLAN SPECIALTY L.P.,0 "MYLAN PHARMACEUTICALS, INC.",0 "MYLAN INSTITUTIONAL, INC",0 MYLAN INSTITUTIONAL INC.,0 "MYLAN CONSUMER HEALTHCARE, INC.",0 MUTUAL PHARMACEUTICAL COMPANY,0 "MORTON GROVE PHARMACEUTICALS, INC",0 "MONARCH PHARMACEUTICALS, INC.",0 MISSION PHARMACAL COMPANY,0 MIKART INC.,0 "NEOLPHARMA, INC.",0 MIDLOTHIAN LABORATORIES,0 Organon LLC,0 "PACIFIC PHARMA, INC.",0 PHYSICIAN THERAPEUTICS LLC,0

PHARMICS INC.,0 "PHARMACYCLICS, INC.".0 PHARMACIA AND UPJOHN COMPANY LLC,0 "PHARMACEUTICAL ASSOCIATES, INC.",0 "PHARBEST PHARMACEUTICALS, INC.".0 "PFIZER, INC.",0 "PFIZER, INC",0 PFIZER LABORATORIES DIV PFIZER INC.,0 PFIZER LABORATORIES DIV PFIZER INC,0 "PERSON & COVEY, INC.",0 PACIFIC PHARMA,0 PERRIGO PHARMACEUTICALS,0 PEDINOL PHARMACAL INC,0 "PARENTA PHARMACEUTICALS, INC.",0 "PAR PHARMACEUTICALS, INC.",0 "PAR PHARMACEUTICAL, INC.",0 "PAR PHARMACEUTICAL, INC",0 PAR PHARMACEUTICAL,0 PAI.0 "PADDOCK LABORATORIES, LLC.",0 "PADDOCK LABORATORIES, INC.",0 PADAGIS US LLC,0 PADAGIS ISRAEL PHARMACEUTICALS LTD.,0 PERRIGO NEW YORK INC.,0 METRICS INC. DBA MAYNE PHARMA,0 METHOD PHARMACEUTICALS,0 MERZ PHARMACEUTICALS,0 LEADER,0 LAURUS LABS LIMITED.0 "LASER PHARMACEUTICALS, LLC",0 "LARKEN LABORATORIES, INC.",0 "LANTHEUS MEDICAL IMAGING, INC.",0 "LANNETT COMPANY, INC.",0 L. PERRIGO COMPANY,0 "KREMERS URBAN, INC.",0 **KREMERS URBAN PHARMACEUTICALS,0** "KONSYL PHARMACEUTICALS, INC.",0 "KING PHARMACEUTICALS, INC.",0 "LEADIANT BIOSCIENCES, INC.",0 "KEDRION BIOPHARMA, INC",0 "JAYMAC PHARMACEUTICALS, LLC",0 JACOBUS PHARMACEUTICALS CO INC.,0 "IVAX PHARMACEUTICALS, INC.",0 **IROKO PHARMACEUTICALS LLC,0** "INTERNATIONAL LABS, INC.",0 "INTERNATIONAL LABORATORIES, LLC".0 "INNOGENIX, LLC",0 "INGENUS PHARMACEUTICALS, LLC",0 **INDIVOR INC.,0** "IMPAX LABORATORIES, INC.",0 "IGI LABORATORIES, INC.",0 "KADMON PHARMACEUTICALS, LLC",0 LEDERLE PIPERACILLIN,0

"LEGACY PHARMACEUTICAL PACKAGING, LLC".0 "LEHIGH VALLEY TECHNOLOGIES, INC.",0 "MEITHEAL PHARMACEUTICALS, INC.",0 "MEDLINE INDUSTRIES, INC.",0 "MEDIMETRIKS PHARMACEUTICALS, INC.",0 "MEDICIS DERMATOLOGICS, INC.",0 "MEDA PHARMACEUTICALS, INC.".0 "MCR-AMERICAN PHARMACEUTICALS, INC.",0 MCKESSON MEDICAL SURGICAL,0 MCKESSON CORPORATION VALU-RITE,0 MCKESSON CORPORATION,0 MCKESSON CORP..0 "MARNEL PHARMACEUTICAL, INC.",0 "MARATHON PHARMAEUTICALS, LLC".0 MALLINCKRODT INC.,0 MAJOR PHARMACEUTICALS.0 "MACOVEN PHARMACEUTICALS, LLC",0 MACLEODS PHARMACEUTICALS LIMITED.0 "MACLEODS PHARMA USA, INC",0 "LUPIN PHARMACEUTICALS, INC.",0 "LUNDBECK, LLC",0 "LNK INTERNATIONAL, INC.",0 LLORENS PHARMACEUTICALS INT'L DIVISION,0 LINEAGE THERAPEUTICS INC.,0 ZYLA LIFE SCIENCES US INC.,0 "LIBERTAS PHARMA, INC. DBA MAYNE PHARMA",0 LEUCADIA PHARMACEUTICALS.0 "PLIVA, INC.",0 ICU MEDICAL INC.,0 "POLY PHARMACEUTICAL CO., INC.",0 "PRAGMA PHARMACEUTICALS, LLC".0 "US WORLDMEDS, LLC",0 "UPSTATE PHARMA, LLC",0 "UPSHER-SMITH LABORATORIES, LLC.".0 "UPSHER-SMITH LABORATORIES, INC.",0 "UCB, INC",0 "UCB MANUFACTURING, INC.",0 U.S. PHARMACEUTICAL CORPORATION,0 "TWi PHARMACEUTICALS, INC.",0 "TWi PHARMACEUTICALS USA, INC.",0 "TWI PHARMACEUTICALS, INC.",0 "TRUPHARMA, LLC",0 VALEANT PHARMACEUTICALS NORTH AMERICA,0 "TRIGEN LABORATORIES, LLC",0 "TORRENT PHARMA, INC.",0 **TOPCO ASSOCIATES LLC,0** "TOLMAR, INC.",0 "TIME-CAP LABS, INC.",0 "TIME CAP LABORATORIES, INC.",0 THE PROCTER & GAMBLE DISTRIBUTING CO.,0

TEVA WOMENS HEALTH INC,0 "TEVA PHARMACEUTICALS USA. INC".0 "TELIGENT PHARMA, INC.",0 "TARO PHARMACEUTICALS USA, INC.",0 "TAGI PHARMA. INC".0 TORRENT PHARMACEUTICALS LIMITED,0 "SUN PHARMACEUTICAL INDUSTRIES, LTD",0 "VALIDUS PHARMACEUTICALS, INC.",0 "VANGARD LABS, INC.",0 ZYDUS PHARMACEUTICALS (USA) INC.,0 XSPIRE PHARMA LLC,0 "XIROMED, LLC.",0 "XGEN PHARMACEUTICALS DJB, INC.",0 "XERIS PHARMACEUTICALS, INC.",0 X-GEN PHARMACEUTICALS,0 WYETH PHARMACEUTICALS INC.,0 WYETH LABORATORIES.0 WYETH CONSUMER HEALTHCARE,0 WOODWARD PHARMA SERVICES LLC.0 "WOMEN'S CHOICE PHARMACEUTICALS, LLC",0 "VALIDUS PHARMACEUTICALS, LLC.",0 "WINDER LABORATORIES, LLC",0 "WG CRITICAL CARE, LLC",0 "WESTMINSTER PHARMACEUTICALS, LLC.",0 WEST-WARD PHARMACEUTICALS CORP.,0 WEST-WARD PHARMACEUTICAL CORP,0 WEST-WARD PHARMACEUTICAL,0 "WATSON PHARMA, INC.",0 WARNER CHILCOTT LABORATORIES.0 WARNER CHILCOTT (US) LLC,0 "VIRTUS PHARMACEUTICALS, LLC",0 "VERTICAL PHARMACEUTICALS, LLC".0 "VENSUN PHARMACEUTICALS, INC.",0 "WILSHIRE PHARMACEUTICALS, INC.",0 SUN PHARMACEUTICAL INDUSTRIES LIMITED,0 SUN PHARMACEUTICAL INDUSTRIES INC.,0 STRIDES PHARMA SCIENCE LIMITED.0 "ROXANE LABORATORIES, INC.",0 ROERIG,0 **ROCHESTER PHARMACEUTICALS,0** "RISING PHARMACEUTICALS, INC",0 "RISING HEALTH, LLC.",0 **RHODES PHARMACEUTICALS L.P.,0** "RENAISSANCE PHARMA, INC.",0 "RECORDATI RARE DISEASES, INC.",0 "RECKITT BENCKISER, INC.",0 "RECKITT BENCKISER PHARMACEUTICALS, INC.".0 "RANBAXY PHARMACEUTICALS, INC.",0 "ROYAL PHARMACEUTICALS, LLC.",0 RANBAXY LABORATORIES INCORPORATED,0 **Ouallent Pharmaceuticals Health,0** "QUINN PHARMACEUTICALS, LLC",0

"OUALITEST PHARMACEUTICALS, INC.".0 PURETEK CORPORATION.0 "PURDUE PRODUCTS, L.P.",0 "PURDUE PHARMA, L.P.",0 "PRUGEN, INC.",0 "PROMIUS PHARMA, LLC",0 "PROMETHEUS LABORATORIES, INC.",0 "PRESTIUM PHARMA, INC.",0 "PRECISION DOSE, INC.",0 **R.A. MCNEIL COMPANY,0 RUGBY LABORATORIES,0** "SANCILIO & COMPANY, INC.",0 SANDOZ.0 STRIDES PHARMA INC.,0 STRATUS PHARMACEUTICALS INC.,0 "STIEFEL LABORATORIES, INC,",0 "STI PHARMA, LLC",0 "SPEC GX, LLC",0 "SPEAR DERMATOLOGY PRODUCTS, INC.".0 "SOLCO HEALTHCARE USA, LLC",0 "SOLCO HEALTHCARE US, LLC",0 "SOLA PHARMACEUTICALS, LLC",0 "SMITH & NEPHEW, INC.",0 "SLATE RUN PHARMACEUTICALS, LLC",0 "SILARX PHARMACEUTICALS, INC.",0 SIGMA-TAU PHARMACEUTICALS,0 "SHIONOGI, INC.",0 SHEFFIELD PHARMACEUTICALS,0 "SETON PHARMACEUTICALS, LLC".0 SELECT BRAND DISTRIBUTORS,0 "SEBELA PHARMACEUTICALS, INC.",0 SDA LABORATORIES.0 "SCIELE PHARMA, INC.",0 "SCIEGEN PHARMACEUTICALS, INC.".0 SCHERING HEALTHCARE PRODUCTS,0 SAVAGE LABORATORIES,0 SANOFI-AVENTIS U.S. LLC,0 SANDOZ INC.,0 "POLY PHARMACEUTICALS, INC.",0 "HOSPIRA, INC.",0 "ZYLERA PHARMACEUTICALS, LLC",0 HOFFMANN-LA ROCHE,0 "COSETTE PHARMACEUTICALS, INC.",0 "APP PHARMACEUTICALS, LLC.",0 "CORIA LABORATORIES, LTD.",0 CONTRACT PHARMACAL CORP,0 COLOPLAST CORPORATION,0 "APTALIS PHARMA US, INC.",0 "COLLEGIUM PHARMACEUTICALS, INC.",0 "COUNTY LINE PHARMACEUTICALS, LLC",0 "ARBOR PHARMACEUTICALS, INC.",0 "COLLEGIUM PHARMACEUTICAL, INC.",0 "COBALT LABORATORIES, INC.",0

"CMP PHARMA, INC.",0 "CIVICA. INC.".0 "CITRON PHARMA, LLC",0 AREVA PHARMACEUTICALS,0 **ARMAS PHARMACEUTICALS INC..0** "ARBOR PHARMACEUTICALS, LLC.",0 "CHAIN DRUG MARKETING ASSOCIATION, INC.".0 COVIS PHARMA S.A.R.L..0 APOLLO PHARMACEUTICALS INC.,0 "DR. REDDY'S LABORATORIES, INC.",0 DOAK DERMATOLOGICS,0 DISTA PRODUCTS CO DIV OF ELI LILLY & CO.0 "DEPO NF SUB, LLC",0 BAXTER HEALTHCARE CORPORATION.0 "ANI PHARMACEUTICALS, INC.",0 DAVA INTERNATIONAL INC.,0 COVIS PHARMA US INC.,0 ANIP ACOUISITION COMPANY,0 "CYPRESS PHARMACEUTICAL, LLC",0 "CUMBERLAND PHARMACEUTICALS, INC.",0 "CUBIST PHARMACEUTICALS, INC.",0 CSL BEHRING LLC,0 "APO-PHARMA USA, INC.",0 CSL BEHRING,0 COVIS PHARMACEUTICALS INC...,0 Concordia Pharmaceuticals Inc.,0 **DUPONT PHARMACEUTICALS,0** "ATON PHARMA. INC.".0 "AUROBINDO PHARMA USA, INC.",0 "HORIZON PHARMA, INC.",0 "BRECKENRIDGE PHARMACEUTICAL, INC.",0 **BRAINTREE LABORATORIES INC.,0 B. BRAUN MEDICAL INC.,0** "BOCA PHARMACAL, LLC",0 **BLUEPOINT LABORATORIES,0** "BIONPHARMA, INC.",0 BRISTOL-MYERS SQUIBB PHARMA CO.,0 **BIONICHE PHARMA,0 BANNER PHARMACAPS INC.,0 BAUSCH & LOMB INC.,0** "BAUSCH HEALTH US, LLC",0 "BAUSCH HEALTH US, LLC.",0 **BEACH PRODUCTS INC,0 BE PHARMACEUTICALS INC.,0** "BAYER HEALTH CARE PHARMACEUTICALS, INC".0 "B. F. ASCHER AND COMPANY, INC.",0 AUROBINDO PHARMA LTD.,0 Akorn Operating Company LLC,0 C B FLEET COMPANY INC,0 "AVENTIS PHARMACEUTICALS, INC.",0 **AVION PHARMACEUTICALS,0**

AVPAK,0 CASPER PHARMA LLC.0 AVRIO HEALTH L.P.,0 AYERST LABORATORIES.0 CAROLINA MEDICAL PRODUCTS COMPANY.0 **BUREL PHARMACEUTICALS,0** "CARDINAL HEALTH 110, LLC. DBA LEADER",0 **AZURITY PHARMACEUTICALS INC.,0** "CAPITAL PHARMACEUTICAL, LLC",0 "CAPELLON PHARMACEUTICALS, LTD.",0 "CAMERON PHARMACEUTICALS, LLC.",0 "CAMBRIDGE THERAPEUTIC TECHNOLOGIES, LLC",0 Advagen Pharma Ltd,0 CAMBER CONSUMER CARE INC.,0 **CARDINAL HEALTH,0** E FOUGERA AND CO.,0 "DAVA PHARMACEUTICALS, INC.",0 "FSC LABORATORIES, INC.",0 "ACTAVIS PHARMA, INC.",0 **GENZYME CORPORATION,0** AJANTA PHARMA LIMITED,0 AKORN INC.0 AKRIMAX PHARMACEUTICALS LLC,0 "GEMINI LABORATORIES, LLC",0 GD. SEARLE LLC DIVISION OF PFIZER INC.,0 "GLENMARK PHARMACEUTICALS, INC., USA",0 "ALAVEN PHARMACEUTICAL, LLC",0 "ALCON LABORATORIES, INC.".0 "G&W LABORATORIES, INC",0 AMICI PHARMACEUTICALS LLC,0 "FRESENIUS KABI USA, LLC".0 FRESENIUS KABI USA LLC,0 "FOREST LABORATORIES, INC.",0 "FERRING PHARMACEUTICALS, INC.",0 GATE PHARMACEUTICALS,0 "FERA PHARMACEUTICALS, LLC",0 "GM PHARMACEUTICALS, INC.",0 ACTAVIS,0 HILLESTAD PHARMACEUTICALS,0 HIKMA PHARMACEUTICALS USA INC.,0 "HIKMA PHARMACEUTICAL USA, INC.",0 ACCORD HEALTHCARE INC.,0 HI-TECH PHARMACAL CO. INC.,0 "HERITAGE PHARMACEUTICALS, INC.",0 "HARRIS PHARMACEUTICAL, INC.",0 **ACTAVIS ELIZABETH LLC,0** "H2-PHARMA, LLC",0 ACCORD HEALTHCARE INCORPORATED,0 **GSK CONSUMER HEALTHCARE,0 GSK CONSUMER HEALTH,0** "GRIFOLS USA, LLC",0 "ACELLA PHARMACEUTICALS, LLC",0

"ACI HEALTHCARE USA, INC.",0 **GREENSTONE LLC.0** GSK CONSUMER HEALTHCARE HOLDINGS (US) LL.0 FALCON PHARMACEUTICALS LTD..0 **BAXTER HEALTHCARE,0** "AMERICAN REGENT, INC.",0 "ALMAJECT, INC.",0 "ENEMEEZ,INC. DBA SUMMIT PHARMACEUTICAL".0 AMERISOURCE BERGEN DRUG CORPORATION,0 "ALLERGAN, INC.",0 ALLERGAN INC,0 AMERISOURCE BERGEN DRUG COMPANY,0 AMERISOURCE BERGEN,0 "EPI HEALTH, LLC",0 ECI PHARMACEUTICALS LLC,0 EPIC PHARMA LLC,0 ECR PHARMACEUTICALS,0 "EXELTIS USA, INC.",0 "AMEDRA PHARMACEUTICALS, LLC",0 EDENBRIDGE PHARMACEUTICALS LLC,0 ALLEGIS PHARMACEUTICALS LLC,0 AMERICAN HEALTH PACKAGING,0 "ESPERO PHARMACEUTICALS, INC.",0 EXELA PHARMA SCIENCES,0 "EXELAN PHARMACEUTICALS, INC",0 "AMERICAN REGENT LABORATORIES, INC.",0 "EDWARDS PHARMACEUTICALS, INC.".0 "ALMATICA PHARMA, INC.",0 "ALMATICA PHARMA, LLC.",0 STRIDES ARCOLAB LIMITED.1 **BARR LABORATORIES INC,1** "AMERIGEN PHARMACEUTICALS, INC.",1 AMGEN/IMMUNEX,1 "TEVA PHARMACEUTICALS USA, INC.",1 ABBVIE INC,1 ABBOTT LABORATORIES,1 AMRING PHARMACEUTICALS INC.,1 "ROUSES POINT PHARMACEUTICALS, LLC",1 **BAXALTA US INC,1 BAXALTA US INC.,1** AMNEAL PHARMACEUTICALS OF NEW YORK LLC.1 "RISING PHARMACEUTICALS, INC.",1 "ANCHEN PHARMACEUTICALS, INC.",1 "SALIX PHARMACEUTICALS, INC.",1 WYETH BIOPHARMA DIVISION OF WYETH,1 "WYETH PHARMACEUTICALS LLC,",1 "VISTAPHARM, INC.",1 STRATEGIC SOURCING SERVICES LLC,1 "ALKERMES, INC.",1 SUN PHARMA GLOBAL FZE,1

ALEMBIC PHARMACEUTICALS INC.,1 "ASCEND LABORATORIES, L.L.C.",1 "SUN PHARMA GLOBAL, INC.",1 "AURIGA LABORATORIES, CORE PHARMA",1 APOTEX CORP..1 "SANOFI-AVENTIS, US LLC",1 **AVENTIS PHARMACEUTICALS,1** "SUN PHARMACEUTICALS INDUSTRIES, INC.",1 ACTIENT PHARMACEUTICALS,1 ALVOGEN INC.,1 "WOCKHARDT AMERICAS, INC.",1 ACTAVIS KADIAN LLC,1 "AMAG PHARMACEUTICALS, INC.",1 WYETH BIOPHARMA,1 SCHERING CORPORATION,1 UNITED THERAPEUTICS CORPORATION,1 "SUN PHARMACEUTICAL INDUSTRIES, INC.",1 AMNEAL PHARMACEUTICALS,1 **BRISTOL-MYERS SOUIBB COMPANY,1** JUBILANT CADISTA PHARMACEUTICALS, INC.".1 **IMPAX GENERICS,1** "GAVIS PHARMACEUTICALS, LLC",1 FRESENIUS MEDICAL CARE NORTH AMERICA,1 "CHAIN DRUG CONSORTIUM, LLC",1 "MAGNA PHARMACEUTICALS, INC.",1 "CIPLA USA, INC.",1 "EON LABS, INC.",1 MAYNE PHARMA INC.,1 **ORGANON USA INC.,1** "NOVEN THERAPEUTICS, LLC.",1 "ENDO PHARMACEUTICALS, INC.",1 NORTHSTAR RX LLC,1 "MCKESSON PACKAGING SERVICE, A DIVISION",1 MYLAN INSTITUTIONAL LLC.,1 **BAXTER US INC,1** MERCK/SCHERING-PLOUGH JV,1 "MEDECOR PHARMA, LLC",1 MERCK SHARP & DOHME LLC,1 MERCK SHARP & DOHME CORP.,1 PARKE-DAVIS DIV OF PFIZER,1 "GENETICS INSTITUTE, INC.",1 "MERCK & CO., INC.",1 "KVK-TECH, INC.",1 "JUBILANT CADISTA PHARMACEUTICALS, INC",1 "GILEAD SCIENCES, INC.",1 CARACO PHARMACEUTICAL LABORATORIES LTD,1 GLAXOSMITHKLINE,1 "PERNIX THERAPEUTICS, LLC",1 **"BAYER HEALTHCARE PHARMACEUTICALS,** INC",1 CADISTA PHARMACEUTICALS INC.,1

PRASCO LABORATORIES,1 "BTA PHARMACEUTICALS, INC.".1 GLOBAL PHARMACEUTICAL CORPORATION,1 **IMMUNEX CORPORATION,1** ELI LILLY AND COMPANY.2 **ACTAVIS INC.,2** "NEXUS PHARMACEUTICALS, INC.",2 MEAD JOHNSON AND COMPANY,2 **TEVA PARENTERAL MEDICINES INC,2 BIOGEN IDEC,2** "E.R. SQUIBB & SONS, INC.",2 "UNICHEM PHARMACEUTICALS (USA), INC.",2 "AMNEAL PHARMACEUTICALS, LLC",2 "E.R. SQUIBB & SONS, LLC.",2 "UCB PHARMA, INC.",2 "EAGLE PHARMACEUTICALS, INC.",2 **BEDFORD LABORATORIES,2** AMGEN USA,2 AMGEN INC.,2 **BAYER HEALTHCARE LLC,2** "JAZZ PHARMACEUTICALS, INC",2 MCKESSON CORPORATION DBA SKY PACKAGING.2 "BIOMARIN PHARMACEUTICAL, INC.",2 SANOFI-SYNTHELABO INC.,2 "SERONO, INC.",2 "GENENTECH, INC.",2 "CAMBER PHARMACEUTICALS, INC.",2 "CELLTRION USA, INC.",2 WALLACE PHARMACEUTICALS,2 "XELLIA PHARMACEUTICALS USA, LLC",2 "ATHENEX PHARMACEUTICAL DIVISION, LLC",2 ASTRAZENECA LP.2 **VIIV HEALTHCARE COMPANY,2** CHARTWELL RX LLC,2 "Teva Pharmaceuticals, Inc.",2 **VIIV HEALTHCARE,2** "OXFORD PHARMACEUTICALS, LLC",2 "MALLINCKRODT, LLC",2 **BOEHRINGER INGELHEIM PHARMACEUTICALS,2** "BIOMARIN PHARMACEUTICALS, INC.",2 STRIDES SHASUN LIMITED,2 ENDO PHARMCEUTICALS SOLUTIONS INC.,2 "ASTELLAS PHARMA US, INC.",2 **ACTAVIS SOUTH ATLANTIC,3** "UCB, INC.",3 EISAI INC.,3 "EXELIXIS, INC.",3 "GALDERMA LABORATORIES, L.P.",3 "EMD SERONO, INC.",3 **ENCUBE ETHICALS PVT. LTD.,3** "AMPHASTAR PHARMACEUTICALS, INC.",3 NOVARTIS,3

"TRIS PHARMA, INC.",3 CIMA LABS.3 **CELGENE CORPORATION,3** "PATRIOT PHARMACEUTICALS, LLC.",3 **QUALITEST PHARMACEUTICALS,3** NOVARTIS PHARMACEUTICALS CORPORATION.3 ASTRAZENECA PHARMACEUTICALS LP.3 "JANSSEN PHARMACEUTICALS, INC",3 **SLAYBACK PHARMA,3** "SAGENT PHARMACEUTICALS, INC.",3 MICRO LABS LIMITED,3 AMNEAL PHARMACEUTICALS LLC.3 "E5 PHARMA, LLC",3 "CROWN LABORATORIES, INC.",3 **BIOGEN INC.,4 BIOGEN IDEC INC..4** "REGENERON PHARMACEUTICALS, INC.",4 AUROMEDICS PHARMA LLC,4 "SIGMAPHARM LABORATORIES, LLC",4 **IPSEN BIOPHARMACEUTICALS,4** AMNEAL BIOSCIENCES,4 "JANSSEN BIOTECH, INC",4 "VERTEX PHARMACEUTICALS, INC.",4 2 "SUPERNUS PHARMACEUTICALS, INC.",4 "DAIICHI SANKYO, INC.",4 "UNICHEM PHARMACEUTICALS, INC.",4 3. VIONA PHARMACEUTICALS INC.,4 "JANSSEN PRODUCTS, LP",4

- FOSUN PHARMA USA.5 "OTSUKA AMERICA PHARMACEUTICALS, INC.",5 **INCYTE CORPORATION,5**
- "OTSUKA AMERICA PHARMACEUTICAL. INC.".5
- **OTSUKA AMERICA.5**
- "CARWIN ASSOCIATES, INC.",5
- NOVITIUM PHARMA LLC,5
- **TAKEDA PHARMACEUTICALS AMERICA INC.,5**
- "JAZZ PHARMACEUTICALS, INC.",5
- LIFESTAR PHARMA LLC,6
- "MILLENNIUM PHARMACEUTICALS, INC.".6
- "TAKEDA PHARMACEUTICALS AMERICA, INC.",6
- "SHIRE US, INC.",6
- WINTHROP U.S.,7
- "NODEN PHARMA USA, INC.",7
- "SOLVAY PHARMACEUTICALS, INC.",7

PAR PHARMACEUTICAL INC.,7 "CEPHALON, INC.".7 ABBVIE INC.,7 PAR PHARMACEUTTICAL INC.,7 SANOFI-AVENTIS U.S.LLC.7 **KARYOPHARM THERAPEUTICS,7** "RITEDOSE PHARMACEUTICALS, LLC",7

Funding This research has no fund.

Data Availability The author has no permission to share data.

Declarations

Competing Interests The author has no conflict of interest.

References

- 1. Data.Gov. Drug Products in the Medicaid Drug Rebate Program. 2023. https://catalog.data.gov/dataset/drug-products-in-the-medic aid-drug-rebate-program-2933e/resource/f25e01e5-10cc-45d8-9eaa-1e4a746ddba1. Accessed 7 Feb 2025.
- Rathore AS, Li Y, Chhabra H, Lohiya A. FDA Warning Letters: A Retrospective Analysis of Letters Issued to Pharmaceutical Companies from 2010-2020. J Pharm Innov. 2022;1-10. Advance online publication.https://doi.org/10.1007/s12247-022-09678-2.
- Ciulla M, Marinelli L, Di Biase G, Cacciatore I, Santoleri F, Costantini A, Dimmito MP, Di Stefano A. Healthcare systems across Europe and the US: the managed entry agreements experience. Healthcare (Basel, Switzerland). 2023;11(3):447. https://doi.org/ 10.3390/healthcare11030447.
- 4. Van Norman GA. Off-label use vs off-label marketing of drugs: part 1: off-label use-patient harms and prescriber responsibilities. JACC Basic Transl Sci. 2023;8(2):224-33. https://doi.org/ 10.1016/j.jacbts.2022.12.011.
- 5. FDA.GOV. Drug Approval Process. 2023. https://www.fda.gov/ media/82381/download. Accessed 7 Feb 2025.
- 6. FDA.GOV. New Drug Application (NDA). 2023. https://www.fda. gov/drugs/types-applications/new-drug-application-nda. Accessed 7 Feb 2025.
- 7. Zettler PJ, Shah SK. Broader implications of eliminating FDA jurisdiction over execution drugs. Am J Public Health. 2021;111(10):1764-7. https://doi.org/10.2105/AJPH.2021. 306425.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.