Universidade de Lisboa

Faculdade de Farmácia / Instituto Superior Técnico

Past Present and Prospective: Drivers of Innovation in Pharma

Gualter Paulo da Silva

Dissertation supervised by Professor Rui Miguel Dias Loureiro and co-supervised by Dra. Ligia Maria Gaspar Ernesto

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Eu, Gualter Paulo Da Silva, declaro ter desenvolvido e elaborado o presente trabalho em consonância com o Código de Conduta e de Boas Práticas da Universidade de Lisboa. Mais concretamente, afirmo não ter incorrido em qualquer das variedades de fraude académica, que aqui declaro conhecer, e que atendi à exigida referenciação de frases, extratos, imagens e outras formas de trabalho intelectual, assumindo na íntegra as responsabilidades da autoria.

Abstract

We explore the key drivers of innovation in the pharmaceutical industry by analyzing R&D (Research and Development) expenditures from Pharmaceutical Research and Manufacturers of America (PhRMA) member companies between 1983 to 2021. Using a PEST (Political, Economic, Social, and Technological) Analysis, the study examines how external factors have influenced the evolution of R&D investments over nearly four decades. The analysis reveals that political factors, such as government policies and regulatory frameworks, have been crucial during periods like the Biotechnology Boom and the COVID-19 pandemic. Economic conditions, including the impact of the Global Financial Crisis, have shown to directly affect R&D expenditures, with recovery, leading to restore growth. Social factors, such as the increasing demand for personalized medicine and public health awareness, have driven shifts in R&D priorities, particularly during the Human Genome Project and the development of mRNA technology. Technological advancements have consistently been the most significant drivers of R&D growth, with breakthroughs in biotechnology and mRNA technology leading to substantial increases in investment. The results highlight the critical role of external factors in shaping the pharmaceutical industry's R&D field, offering insights into future trends and strategic considerations. This study highlights the importance in navigating with the usage of PEST factors to sustain innovation and maintain a competitive edge in the industry.

Keywords: Pharmaceutical Innovation; R&D Expenditures; PEST Analysis; Innovation Drivers; Technological Advancements

Resumo

Exploramos os principais motores da inovação na indústria farmacêutica através da análise dos investimentos em I&D (Investigação e Desenvolvimento) dos membros da Organização Pharmaceutical Research and Manufacturers of America (PhRMA) entre 1983 e 2021. Utilizando uma análise PEST (Política, Económica, Social e Tecnológica), examinamos como os fatores externos influenciaram a evolução dos investimentos em I&D ao longo de quase quatro décadas. A análise revela que fatores políticos, como as políticas governamentais e normas regulatórias, foram cruciais durante períodos como o *Boom* da Biotecnologia e a pandemia COVID-19. As condições económicas, incluindo o impacto da Crise Financeira Global, mostraram afetar diretamente os gastos em I&D, com a recuperação levando ao restabelecimento do crescimento. Fatores sociais, como o aumento da procura por medicina personalizada e a sensibilização para a saúde pública, impulsionaram mudanças nas prioridades de I&D, particularmente durante o Projeto Genoma Humano e o desenvolvimento da tecnologia de mRNA. Os avanços tecnológicos têm sido consistentemente os motores mais significativos do crescimento em I&D, com avanços na biotecnologia e na tecnologia de mRNA a conduzir a aumentos substanciais no investimento. Os resultados destacam o impacto de fatores externos no investimento I&D da indústria farmacêutica, oferecendo prespectivas sobre tendências futuras e potenciais considerações estratégicas. Este estudo destaca a importância da utilização dos fatores PEST para sustentar a inovação e manter uma vantagem competitiva na indústria.

Palavras-chave: Inovação Farmacêutica; Despesas em I&D; Análise PEST; Motores de Inovação; Avanços Tecnológicos

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AI - Artificial Intelligence
CAGR - Compound Annual Growth Rate
PEST Analysis - Political Economic Social Technology Analysis
PhRMA - Pharmaceutical Research and Manufacturers of America
R&D - Research and Development
SWOT - Strengths, Weaknesses, Opportunities, and Threats Analysis

1. Introduction

1.1 Historical Overview of Pharmaceutical Innovation

The evolution of pharmaceutical innovation has been marked by transformative discoveries and advancements that have fundamentally altered the healthcare sector. This historical overview shows the significant milestones in the industry, from the discovery of penicillin(1) to the rapid development of mRNA technology that led to the rapid development in the COVID-19 vaccine during the pandemic (2). By understanding these pivotal moments, we can better analyze the trends in R&D expenditures by PhRMA member companies from 1983 to 2021(annex 1)(3).

1.1.2 Pharmaceutical R&D and PhRMA Member Companies

The pharmaceutical industry plays a crucial role in advancing global health, with innovation being the core (4). Research and Development (R&D) is the heart of this innovation, driving the discovery and development of new therapies that address undelivered medical needs. Among the important pieces in this space are the members of the Pharmaceutical Research and Manufacturers of America (PhRMA)(5), which represent the leading biopharmaceutical companies in the world. PhRMA member companies are responsible for the majority of new drug discoveries, with substantial investments in R&D showing their commitment to innovation.

From 1983 to 2021, R&D expenditures by PhRMA member companies have shown significant growth, reflecting the industry's continuous efforts to advance medical science(3) .This period witnessed substantial fluctuations in R&D expenditures, influenced by various external factors that have either drove or restrained innovation. The analysis of these expenditures provides valuable insights into the dynamics of pharmaceutical R&D and highlights the important role of PhRMA member companies in shaping the industry's future.

1.1.3 Early Discoveries and Modern Pharmaceuticals (1928-1982)

The history of pharmaceutical innovation began with early discoveries that setup the modern medicine. The discovery of penicillin by Alexander Fleming in 1928(1) is widely regarded as one of the most significant medical discoveries of the 20th century. Fleming's discovery not only revolutionized the treatment of bacterial infections but also marked the beginning of the antibiotic era, which saved millions of lives and drastically reduced mortality from infectious diseases.

During the mid-20th century, the pharmaceutical industry saw a surge in innovation, driven by the development of vaccines and other essential drugs. An example, the introduction of the

polio vaccine in the 1950s led to a significant reduction in the incidence of poliomyelitis, a devastating disease that caused paralysis and death (6). Similarly, the development of oral contraceptives in the 1960s had huge social and economic impacts, empowering women to control their reproductive health and contributing to the feminist movement (7).

This era also witnessed the establishment of regulatory frameworks to ensure the safety, efficacy, and quality of pharmaceuticals. The 1962 Kefauver-Harris Amendments to the U.S. Food, Drug, and Cosmetic Act (8), for example, required drug manufacturers to provide evidence of the effectiveness and safety of their products before they could be sent to the market. This regulatory milestone led to create a base for future pharmaceutical innovation by establishing rigorous standards for drug approval.

1.1.4 Biotechnology Boom (1983-1990)

The 1980s marked the beginning of the biotechnology revolution, a period of explosive growth driven by advances in genetic engineering and molecular biology. One of the most significant developments during this time was the approval of the first genetically engineered drug, insulin, in 1982 (9). This breakthrough demonstrated the potential of recombinant DNA technology to produce therapeutic proteins and paved the way for the development of other biopharmaceuticals.

The biotechnology boom was characterized by the rise of biotech firms that focused on developing novel therapies using innovative technologies. Monoclonal antibodies, for example, emerged as a promising class of therapeutics with applications in cancer treatment, autoimmune diseases, and other conditions (10). Gene therapy, which aims to correct genetic defects by introducing or modifying genes within a patient's cells, also gained momentum during this period (11).

This surge in innovation led to a significant increase in R&D expenditures. Pharmaceutical companies and biotech firms invested heavily in research to develop new drugs and therapies, leading to the establishment of the modern biotechnology industries.

1.1.5 Human Genome Project (1990-2003)

The Human Genome Project (HGP), initiated in 1990 and completed in 2003, was one of the most ambitious and impactful scientific attempts of the 20th century. The project aimed to map the entire human genome, identifying all the genes and their functions. The successful completion of the HGP revolutionized our understanding of human biology and disease, providing the foundation for the era of personalized medicine (12).

The insights gained from the HGP had profound implications for pharmaceutical R&D. By identifying genetic variations associated with diseases, researchers could develop targeted

therapies to individual patients' genetic profiles. This approach not only improved the efficacy of treatments but also reduced the risk of adverse effects, leading to better patient outcomes.

In addition to advancing personalized medicine, the HGP encouraged the growth of bioinformatics, a field that combines biology, computer science, and information technology to analyze and interpret biological data. The integration of data-driven approaches into drug discovery and development became a hallmark of this period, leading to more efficient and effective R&D processes.

1.1.6 Financial Crisis and Recovery (2003-2010)

The global financial crisis of 2008 had a significant impact on the pharmaceutical industry, leading to a period of economic uncertainty and tightened budgets. As a result, many pharmaceutical companies were forced to reassess their R&D investments, focusing on cost-cutting measures and strategic realignments.

Despite the challenges posed by the financial crisis, the industry demonstrated resilience. Pharmaceutical companies adopted various strategies to maintain innovation while managing costs like increasing efficiency through outsourcing. Numerous major pharmaceutical and biotech companies have been actively enhancing their capabilities and increasingly focusing on efficiency, cost-effectiveness, and productivity, as evidenced by several leading pharmaceutical companies, where none experienced bankruptcy or required substantial government assistance. By the early 2010s, the industry had begun to recover, with R&D investments returning to pre-crisis levels. This recovery was marked by a renewed focus on high-value therapeutic areas, such as oncology and rare diseases, where the potential for breakthrough treatments was greatest. The financial crisis and subsequent recovery period highlighted the industry's ability to adapt to economic pressures while continuing to innovate. (13,14).

1.1.7 mRNA Technology and mRNA Vaccines (2010-2015)

The period from 2010 to 2015 marked a significant turning point in pharmaceutical innovation with the emergence of mRNA technology and mRNA vaccines. These technologies offered a new approach to vaccine development, with the potential to create rapid and scalable vaccines for infectious diseases.

Unlike traditional vaccines, which use weak or inactivated pathogens, mRNA vaccines work by introducing a small piece of genetic material (mRNA) into the body (15). This mRNA instructs cells to produce a protein that triggers an immune response, effectively training the immune system to recognize and fight the actual pathogen if it is encountered later.

During this period, significant advancements were made in understanding and applying mRNA technology. While the technology was still in its early stages, it showed great promise for use

in a wide range of applications, including cancer immunotherapy and infectious disease prevention. The foundational work done during this time would later prove crucial in the rapid development of COVID-19 vaccines in 2020 (16).

R&D expenditures during this period reflected the growing interest and investment in these innovative technologies. Pharmaceutical companies and biotech firms recognized the potential of mRNA technology and began to move resources toward its development, in order to be prepared for future breakthroughs.

1.1.8 Recent Growth and COVID-19 (2015-2021)

The most recent period, from 2015 to 2021, has been marked by substantial growth in pharmaceutical R&D, driven by advancements in technology and the global response to the COVID-19 pandemic. The rapid development of mRNA vaccines, such as those produced by Pfizer-BioNTech and Moderna, highlighted the industry's ability to innovate quickly in the face of a global health crisis (17) .

The COVID-19 pandemic presented unprecedented challenges, forcing pharmaceutical companies to accelerate their R&D efforts. The collaboration between governments, international organizations, and the private sector played a critical role in the development and distribution of vaccines. The pandemic also showed the importance of digital health technologies, with telemedicine, remote monitoring, and AI-driven drug discovery gaining prominence during this period (18).

R&D expenditures during this time reached new heights, reflecting the urgent need for innovative solutions to combat the pandemic. The lessons learned from the COVID-19 response are likely to shape the future of pharmaceutical innovation.

1.1.9 Timeline in Pharmaceutical Innovation (1983-2021)

Figure 1. Timeline of Key Events in Pharmaceutical Innovation (1983-2021)

As illustrated in Figure 1. the major achievements in pharmaceutical innovation from 1983 to 2021, divided into five key periods: the Biotechnology Boom, the Human Genome Project, the Financial Crisis and Recovery, mRNA Technology and mRNA Vaccines, and Recent Growth and COVID-19. Each key period highlights significant events that have driven advancements in the pharmaceutical industry, influencing R&D expenditures and shaping the future of healthcare (10,13,14,17,19,20,21),

1.2 Key Events and Their Impact on R&D Expenditures

To understand the evolution of R&D expenditures, it is essential to examine the key historical events that have shaped the pharmaceutical landscape. Several distinct periods stand out, each characterized by specific developments that had a profound impact on R&D investments:

Biotechnology Boom (1983-1990): This era marked the rise of biotechnology, driven by advances in genetic engineering and favorable government policies. The resulting increase in R&D spending was a direct response to the new opportunities presented by these technological breakthroughs.

Human Genome Project (1990-2003): The mapping of the human genome during this period opened new avenues for personalized medicine and genomics, leading to increased R&D investments in these innovative areas.

Financial Crisis and Recovery (2003-2010): The global financial crisis of 2008 temporarily constrained R&D expenditures, but subsequent recovery efforts, supported by strategic government interventions, helped restore growth in R&D investments.

RNA Technology and mRNA Vaccines (2010-2015): The early development of mRNA technology, which later played an important role in the COVID-19 pandemic, underscored the importance of sustained investment in innovative technologies.

Recent Growth and COVID-19 Response (2015-2021): The COVID-19 pandemic prompted an unprecedented surge in R&D spending, particularly in vaccine development, highlighting the pharmaceutical industry's ability to rapidly respond to global health crises.

1.3 PEST Analysis: A Framework for Understanding External Factors

While the key events provide a chronological perspective on R&D expenditures, a PEST (Political, Economic, Social, and Technological) analysis offers a structured approach to understanding the external influences that have shaped these trends (22). Each of these factors plays a distinct role in driving R&D investments:

Political Factors: Government policies, regulatory frameworks, and international collaborations have been crucial in determining the pace and direction of R&D spending. Key political decisions, such as the Orphan Drug Act(21) and accelerated regulaory approvals during the COVID-19 pandemic, have had a significant impact on innovation.

Economic Factors: The economic environment, including periods of prosperity and downturns, has directly influenced the availability of capital for R&D. Economic resilience, particularly during and after the financial crisis, has been essential for sustaining R&D growth.

Social Factors: Public health awareness, social demand for new therapies, and the push for personalized medicine have guided the focus of R&D efforts. Social factors have

driven the industry's response to global health needs, as seen during the Human Genome Project and the COVID-19 pandemic.

Technological Factors: Technological advancements have consistently been the most significant drivers of R&D growth. Breakthroughs in biotechnology, genomics, and mRNA technology have not only increased R&D expenditures but also transformed the pharmaceutical landscape.

The following sections will present a detailed analysis of R&D expenditures by PhRMA member companies, segmented by the key historical events and evaluated through the PEST Analysis. This approach will provide a comprehensive understanding of how external factors have shaped the pharmaceutical industry's innovation landscape and offer insights into future trends.

2. Data and Methods

2.1 Data Source

The analysis in this thesis is based on the historical R&D expenditure data of PhRMA member companies from 1983 to 2021(3). The data covers expenditures in three categories: Total R&D Expenditures, Domestic R&D Expenditures, and R&D Expenditures Abroad. The data was sourced from industry reports and historical records, providing a comprehensive view of the industry's investment trends over nearly four decades.

2.2 Data Analysis Methods

To analyze the R&D expenditure trends, the data was organized chronologically and segmented into five key periods based on significant historical events and phases in the pharmaceutical industry. Each key period was carefully selected to capture notable shifts in R&D spending patterns influenced by various external factors such as technological advancements, economic conditions, and regulatory changes.

The key periods identified for analysis are:

Biotechnology Boom (1983-1990): Marked by advancements in genetic engineering and the introduction of biotechnology firms, which significantly influenced R&D investments.
Human Genome Project (1990-2003): A period of substantial investment in genomics and personalized medicine, driven by the mapping of the human genome.
Financial Crisis and Recovery (2003-2010): Characterized by a temporary dip in R&D spending due to economic constraints, followed by a recovery as financial conditions improved.
RNA Technology and mRNA Vaccines (2010-2015): Highlighting the emergence of RNA-based technologies and their impact on R&D expenditures, particularly in the context of vaccine development.
Recent Growth and COVID-19 (2015-2021): Reflecting the rapid increase in R&D spending in response to the global pandemic, with a focus on vaccine research and development.

2.3 Methodological Approach

Trend Analysis: For each key period, the trend in R&D expenditures was analyzed to identify overall growth patterns, significant peaks, and troughs. The analysis includes:

Compound Annual Growth Rate (CAGR): Calculated for each period to quantify the average annual growth rate of R&D expenditures.
Moving Averages: Applied to smooth out short-term fluctuations and highlight long-term trends in the data.
Peak and Trough Identification: Specific years with significant increases (peaks) or decreases (troughs) in R&D spending were identified and analyzed in relation to external events or industry developments.

Zoomed-In Graphs: For each key period, detailed graphs were generated to visualize the R&D expenditure trends. These graphs display:

Total R&D Expenditures, **Domestic R&D Expenditures**, and **R&D Expenditures Abroad**.
Moving Averages to provide a clearer view of the overall trend.
Significant peaks and troughs to facilitate easy identification and discussion of critical points in the data.
Correlation with Historical Events and Regulatory Changes: The trends, peaks, and troughs in R&D expenditures were correlated with significant historical events, technological advancements, and regulatory changes that occurred during each key period. This correlation helps explain the underlying reasons for changes in investment patterns.

2.4 Interpretation and Discussion

The results of the analysis are discussed in the context of each key period. The discussion focuses on:

The **trends** observed in R&D expenditures and how they align with historical events.
The **impact of specific factors** such as technological breakthroughs, economic crises, or regulatory support on R&D investments.
The **implications** of these trends for the pharmaceutical industry, including the challenges and opportunities during each period.

2.5 PEST Analysis: Impact of External Factors on R&D Investments

In addition to the trend analysis, includes a comprehensive examination of the impact of external Political, Economic, Social, and Technological (PEST) factors on R&D expenditures

from 1983 to 2021. This analysis provides a deeper understanding of the broader forces that shaped investment decisions over the past several decades.

By employing this method, the thesis provides a comprehensive understanding of how external factors have influenced R&D expenditures over time, offering insights into the strategic decisions made by PhRMA member companies in response to changing conditions.

3. Results and Discussion

3.1 Overview of R&D Expenditure Trends

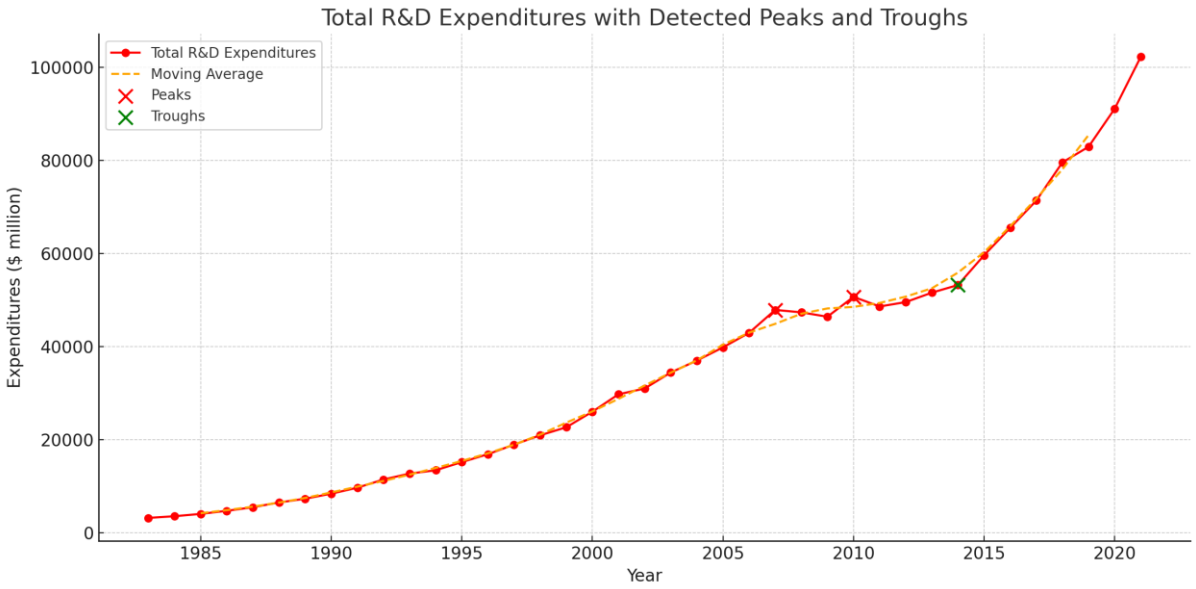
In this segment we present the analysis of R&D expenditures by PhRMA member companies from 1983 to 2021(3). The analysis includes trends, significant peaks, and troughs in expenditures, and the correlation of these trends with historical events and regulatory changes. The results are visualized through a series of graphs that illustrate the annual R&D expenditures, highlighting key periods of growth and decline. The Compound Annual Growth Rate (CAGR) is calculated to provide a comprehensive understanding of the growth patterns in R&D investments.

We'll divide the analysis into Total, Domestic and Abroad R&D expenditures, taking into account the meanings provided (3):

> **Total R&D:** Combines both domestic and abroad R&D expenditures,
> **Domestic R&D:** Expenditures within the United States by all PhRMA member companies.
> **R&D Abroad:** Spending outside the U.S. by U.S.-owned PhRMA companies and overseas R&D by U.S. affiliates of foreign-owned PhRMA companies, excluding foreign divisions of foreign-owned companies.

3.2 Trends in R&D Expenditures

3.2.1 Total R&D Expenditures with detected Peaks and Troughs



Graph 1. Total R&D Expenditures by PhRMA Member Companies (1983-2021).

As we can see Graph 1. illustrates the total R&D expenditures by PhRMA member companies from 1983 to 2021. The red line represents the annual expenditures in million dollars, indicating a general upward trend over the period. The moving average is represented by a

smoother orange curve, which helps highlight the underlying trend by mitigating short-term fluctuations.

One can consider the following key points of interest, including the detected peaks and troughs

> **Peaks** are marked with red crosses (X) and signify periods where R&D expenditures reached local maximum. These peaks often correspond to significant events or regulatory changes impacting R&D investment.
> **Troughs** are marked with greens crosses (X) and indicate periods where expenditures hit local minimum, reflecting potential slowdowns in investment due to various factors such as economic decline or shifts in market dynamics

CAGR Calculation

The CAGR (Compound Annual Growth Rate) formula is used to calculate the annual growth rate of an investment over a specified period of time, assuming the growth is compounded annually. The formula is given by (23):

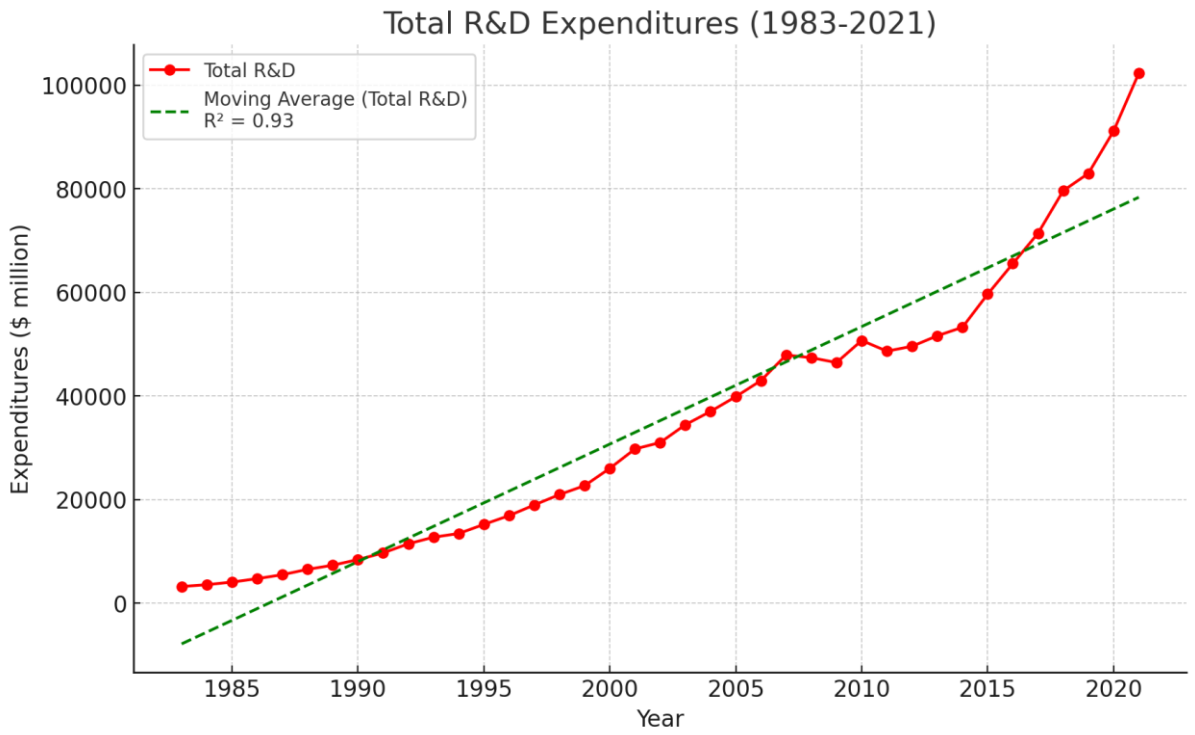
$$\text{CAGR} = \left(\frac{\text{Ending Value}}{\text{Beginning Value}}\right)^{\frac{1}{\text{Number of Years}}} - 1 \quad (23)$$

> **Ending Value** is the value at the end of the period.
> **Beginning Value** is the value at the beginning of the period.
> **Number of Years** is the duration over which the growth is calculated.

$$\text{CAGR}_{\text{Total}} = \left(\frac{102{,}288.4}{3{,}217.6}\right)^{\frac{1}{38}} - 1 \approx 0.0953 \text{ or } 9.53\% \quad (23)$$

The CAGR for total R&D expenditures from 1983 to 2021 is approximately 9.5%, indicating robust growth driven by scientific advancements, regulatory incentives, and market demand.

3.2.2 R-Value for Total R&D Expenditures

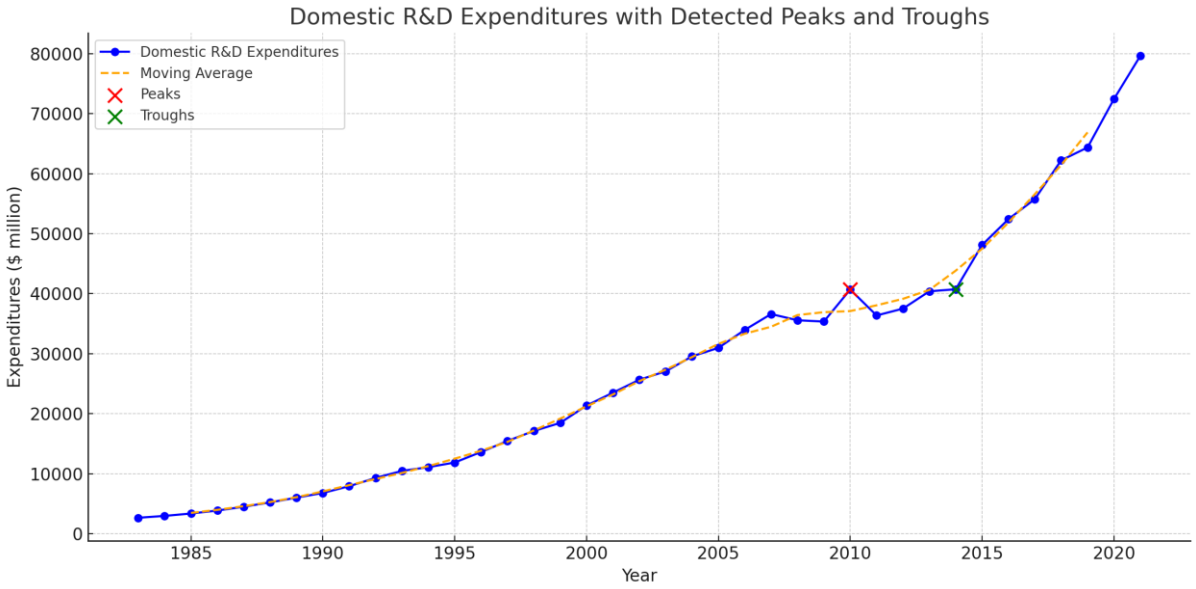


Graph 2. R- Value for Total R&D Expenditures by PhRMA Member Companies (1983-2021). This figure illustrates the total R&D expenditures by PhRMA member companies from 1983 to 2021, measured in million dollars. The red line represents the annual expenditures, showing a clear and substantial upward trend over the period.

Overall Trend: The graph shows a strong upward trajectory in R&D expenditures, reflecting consistent growth over the nearly four-decade period.

R-Squared Value: The R-squared value of 0.93, indicated in the graph, suggests a very high correlation and good fit for the linear trend line applied to the data. This implies that 93% of the variance in R&D expenditures can be explained by the time variable, signifying a strong linear relationship between the years and the investment levels.

3.2.3 Domestic R&D Expenditures with detected Peaks and Troughs



Graph 3. Domestic R&D Expenditures by PhRMA Member Companies (1983-2021)

This figure presents the domestic R&D expenditures by PhRMA member companies from 1983 to 2021. The blue line represents the annual expenditures in million dollars within the United States, showing a clear upward trend over the period. The moving average, showed by a smoother orange curve, highlights the underlying trend by reducing short-term fluctuations.

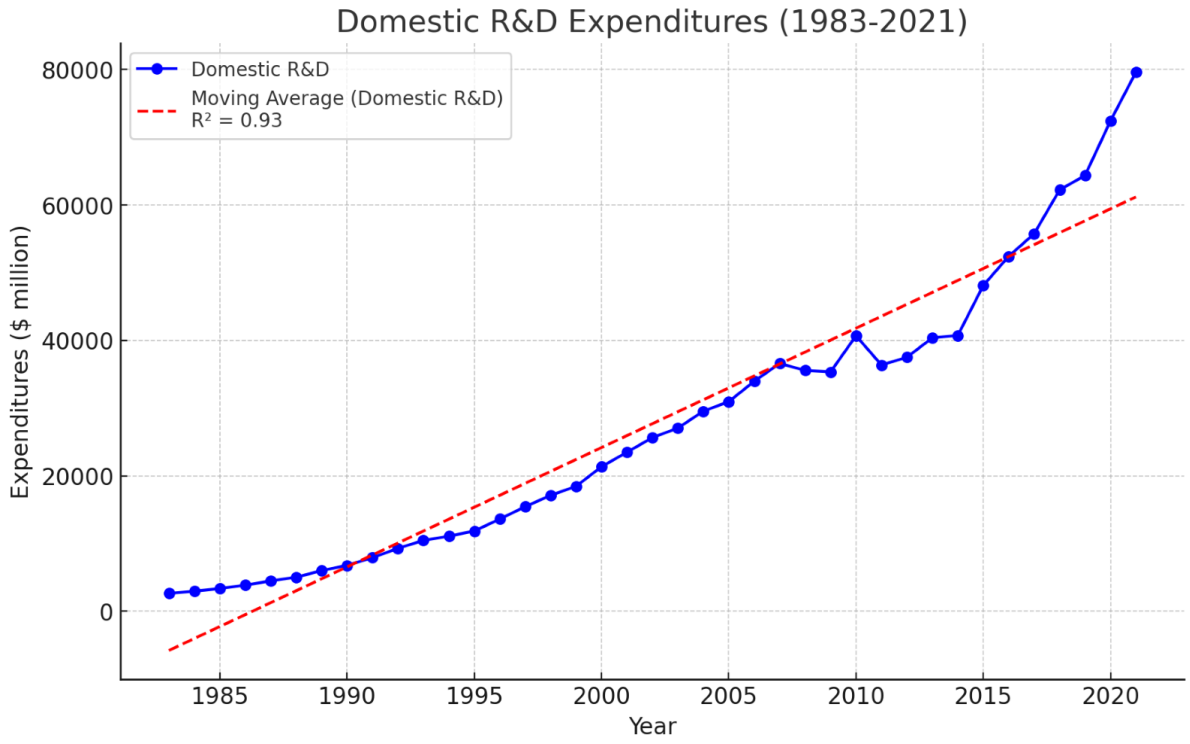
CAGR Calculation

$$\text{CAGR}_{\text{Domestic}} = \left(\frac{79{,}610.0}{2{,}671.3}\right)^{\frac{1}{38}} - 1 \approx 0.0934 \text{ or } 9.34\% \quad (23)$$

The Compound Annual Growth Rate (CAGR) value of 9.34% for Domestic R&D Expenditures signifies a robust and consistent growth rate over the specified period. A CAGR of 9.34% indicates that domestic R&D expenditures have grown at an average annual rate of 9.34% from 1983 to 2021.

This consistent growth rate suggests a sustained commitment by PhRMA member companies to invest in research and development activities within the United States.

3.2.4 R-Value for Domestic R&D Expenditures

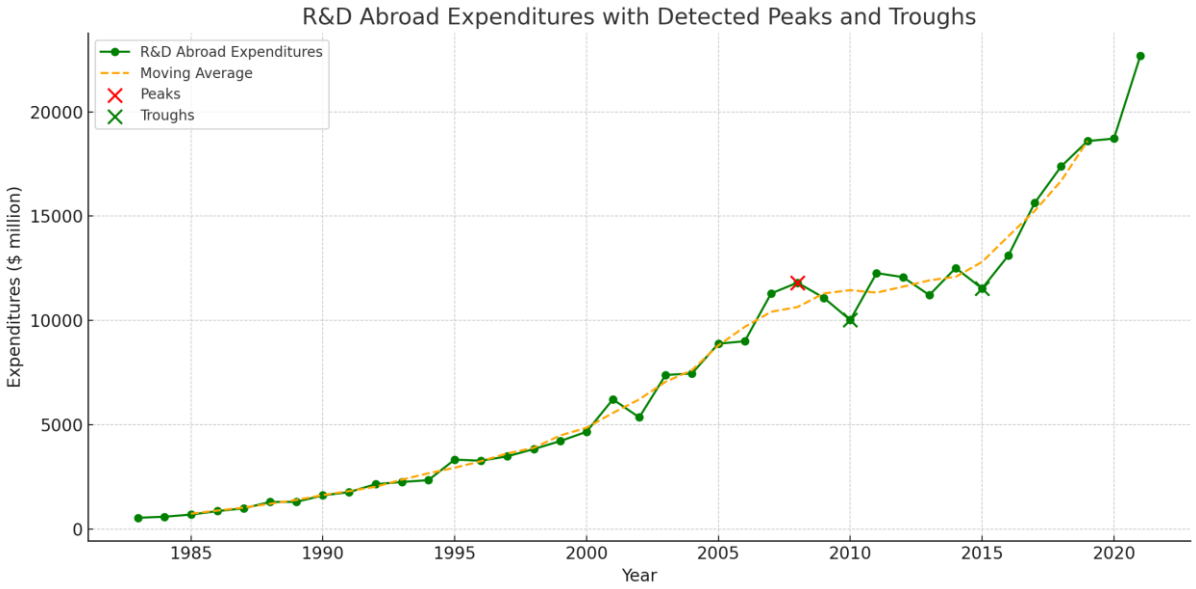


Graph 4: R- Value for Domestic R&D Expenditures by PhRMA Member Companies (1983-2021).

Overall Trend: The graph shows a strong and consistent increase in domestic R&D expenditures, indicating a steady commitment to research and development activities within the United States.

R-Squared Value (R^2): The R-squared value of 0.93 is prominently displayed, representing the proportion of variance in R&D expenditures that can be explained by the year. An R^2 value of 0.93 suggests a very strong linear relationship, indicating that 93% of the variability in domestic R&D expenditures is explained by the passage of time.

3.2.5 Abroad R&D Expenditures with detected Peaks and Troughs



Graph 5. Abroad R&D Expenditures by PhRMA Member Companies (1983-2021)

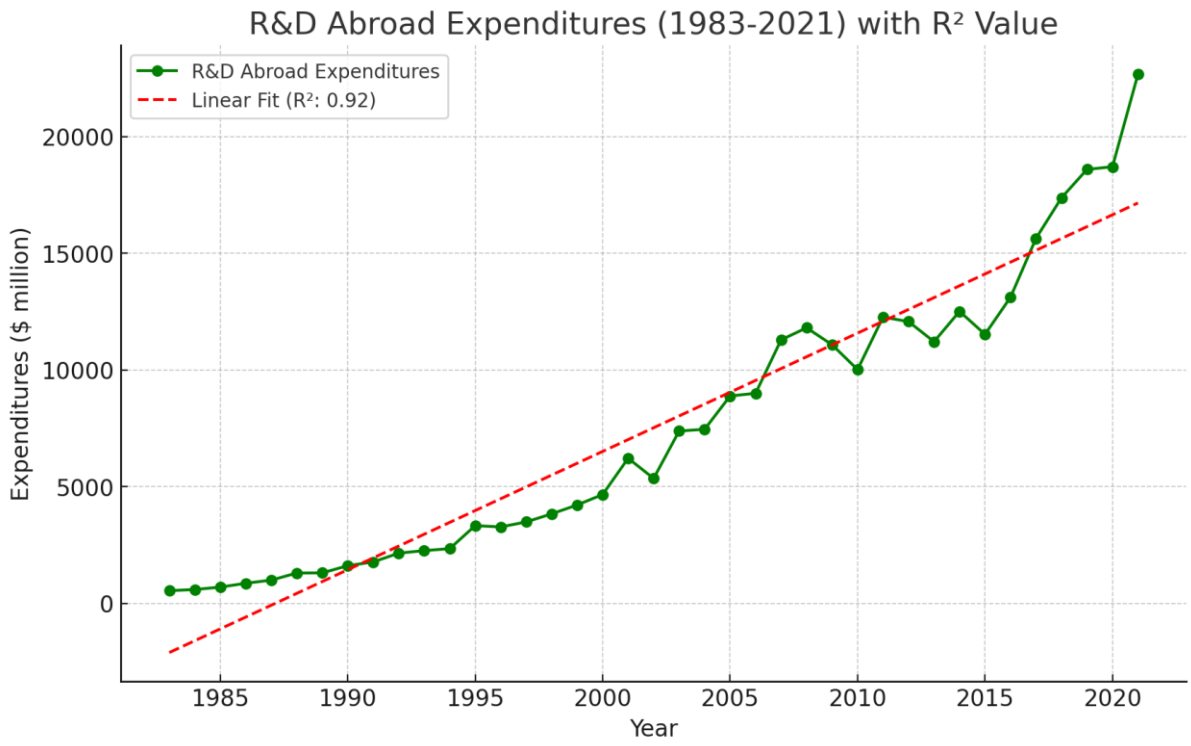
This figure illustrates the R&D expenditures abroad by PhRMA member companies from 1983 to 2021, measured in million dollars. The green line represents the annual expenditures, showing the trend over the period, while the moving average, shown by the smoother yellow line, highlights the underlying trend by reducing short-term fluctuations.

CAGR Calculation

$$\text{CAGR}_{\text{Abroad}} = \left(\frac{22{,}678.4}{546.3}\right)^{\frac{1}{38}} - 1 \approx 0.1030 \text{ or } 10.30\% \quad (23)$$

The Compound Annual Growth Rate (CAGR) value of 10.30% for Abroad R&D Expenditures signifies a robust and accelerated growth rate over the specified period. A CAGR of 10.30% indicates that the R&D expenditures abroad have grown at an average annual rate of 10.30% from 1983 to 2021. This high growth rate reflects the increasing importance and investment in international research and development by PhRMA member companies.

3.2.6 R-Value for Abroad R&D Expenditures



Graph 6. R- Value for Abroad R&D Expenditures by PhRMA Member Companies (1983-2021).

Overall Trend: The graph displays a consistent upward trajectory in R&D Abroad expenditures from 1983 to 2021, reflecting a significant and sustained increase in investment by PhRMA member companies in research and development activities outside the United States. This growth highlights the global expansion and increasing importance of international R&D efforts within the pharmaceutical industry over the nearly four decades analyzed.

R-Squared Value (R^2): The R-squared value of 0.92 is prominently displayed, representing the proportion of variance in R&D Abroad expenditures that can be explained by the year. An R^2 value of 0.92 indicates a very strong linear relationship, suggesting that 92% of the variability in R&D Abroad expenditures is explained by the passage of time. This high R^2 value underscores the strong correlation between time and the increasing trend in abroad R&D investments, reflecting the industry's consistent and growing focus on international research initiatives.

4. Analysis of Key Periods

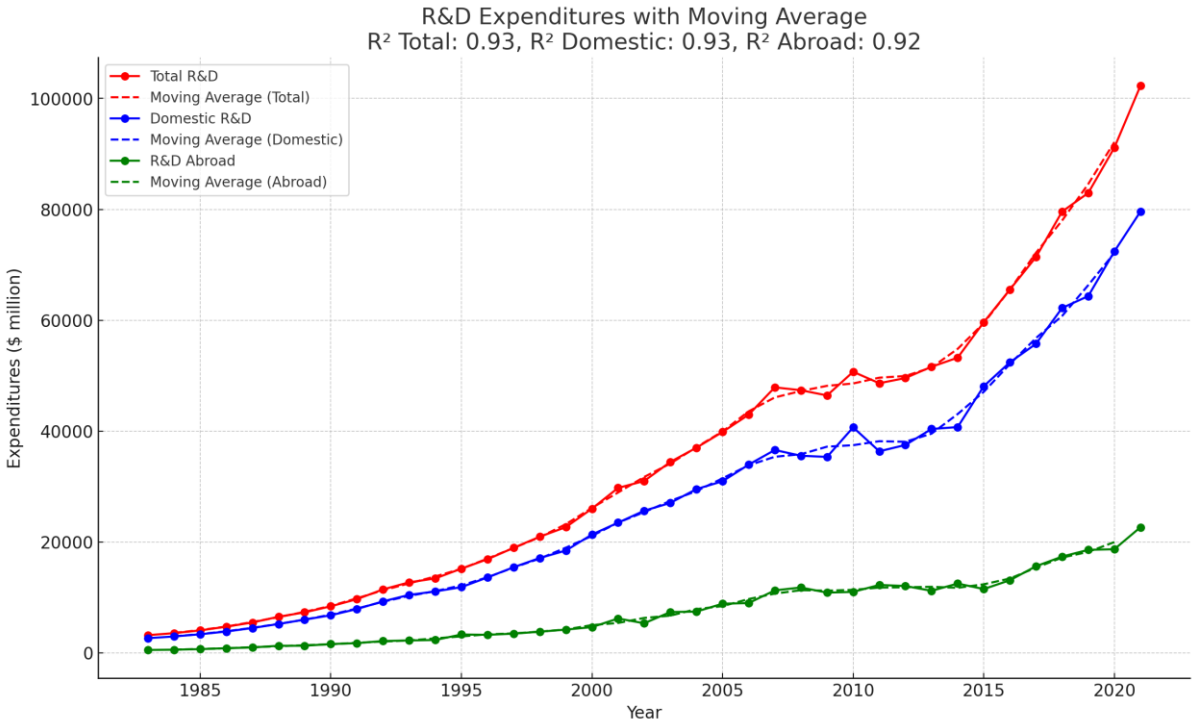
This method allows to identify and discuss significant trends, peaks, and troughs within those periods. By focusing on these intervals, we can obtain detailed insights into what drove changes in investment, whether they were related to scientific breakthroughs, economic conditions, or other factors.

Identify Key Periods: Break-down the entire timeline into smaller, meaningful periods based on historical events or phases in the industry.

Biotechnology Boom (1983-1990):
Human Genome Project (1990-2003)
Financial Crisis and Recovery (2003-2010)
mRNA Technology and mRNA Vaccines (2010-2015)
Recent Growth and COVID-19 (2015-2021)

Create Zoomed-In Graphs: For each key period, detailed graphs highlighting R&D expenditures (total, domestic, and abroad) with clearly peaks and troughs.

Analyze Each Period: Discuss the trends within each period, focusing on significant peaks and troughs. Explain potential reasons for these changes, such as technological advancements, regulatory changes, economic conditions, or major health crises.



Graph 7. All R&D Expenditures by PhRMA Member Companies (1983-2021)

This figure presents the total R&D expenditures by PhRMA member companies from 1983 to 2021, measured in million dollars. It includes domestic R&D expenditures, R&D expenditures abroad, and the combined total R&D expenditures. The data points for each category are connected by lines of different colors:

Blue Line: Domestic R&D expenditures.
Green Line: R&D expenditures abroad.
Red Line: Total R&D expenditures, which is the sum of domestic and abroad expenditures.
Dashed Lines: Represent the moving averages for each category, providing a smoothed trend over the analyzed period.

Overall Trend

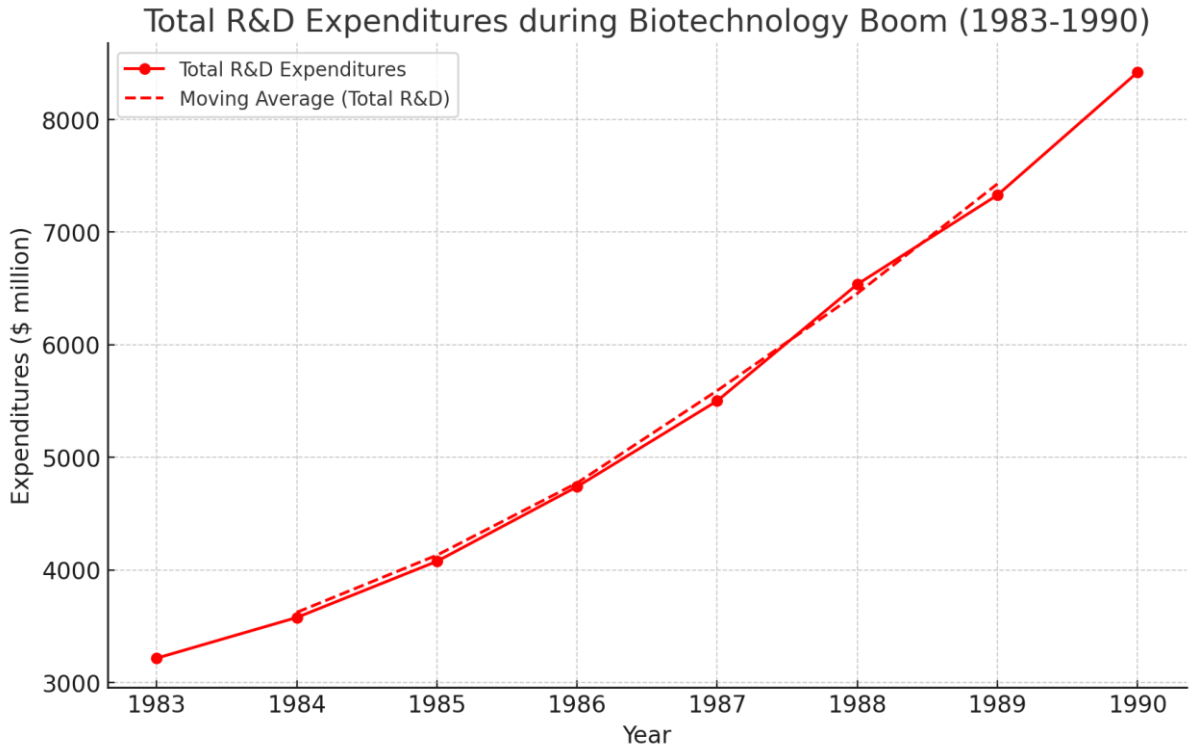
The graph shows a clear upward trajectory for all three categories, indicating consistent growth in R&D investments over the analyzed period.
The total R&D expenditures (red line) exhibit the most significant growth, reflecting the combined contributions of both domestic and abroad investments.
The moving averages (dashed lines) smooth out the short-term fluctuations, highlighting the long-term trend of increasing R&D expenditures.

R-Squared Values (R^2):

R^2 Total: 0.93
R^2 Domestic: 0.93
R^2 Abroad: 0.92

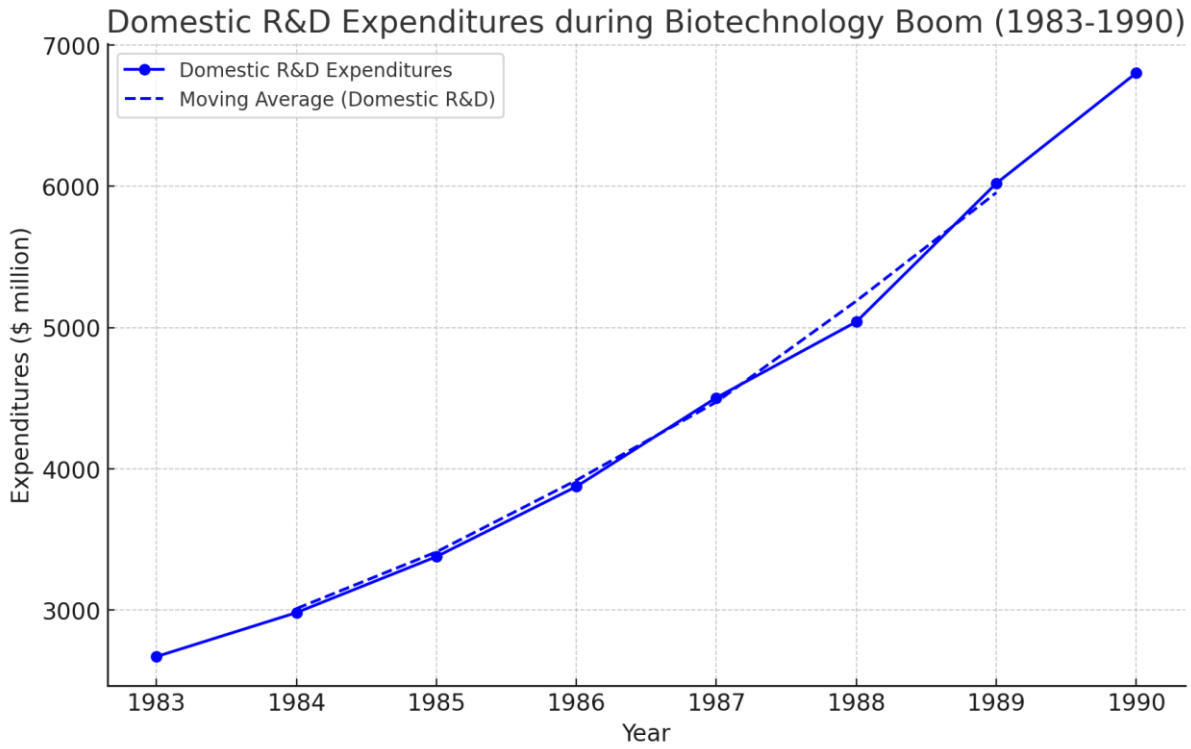
These high R-squared values indicate a very strong correlation between time and R&D expenditures for all categories, suggesting that the model explains a high proportion of the variance in the data

4.1 Biotechnology Boom (1983-1990)



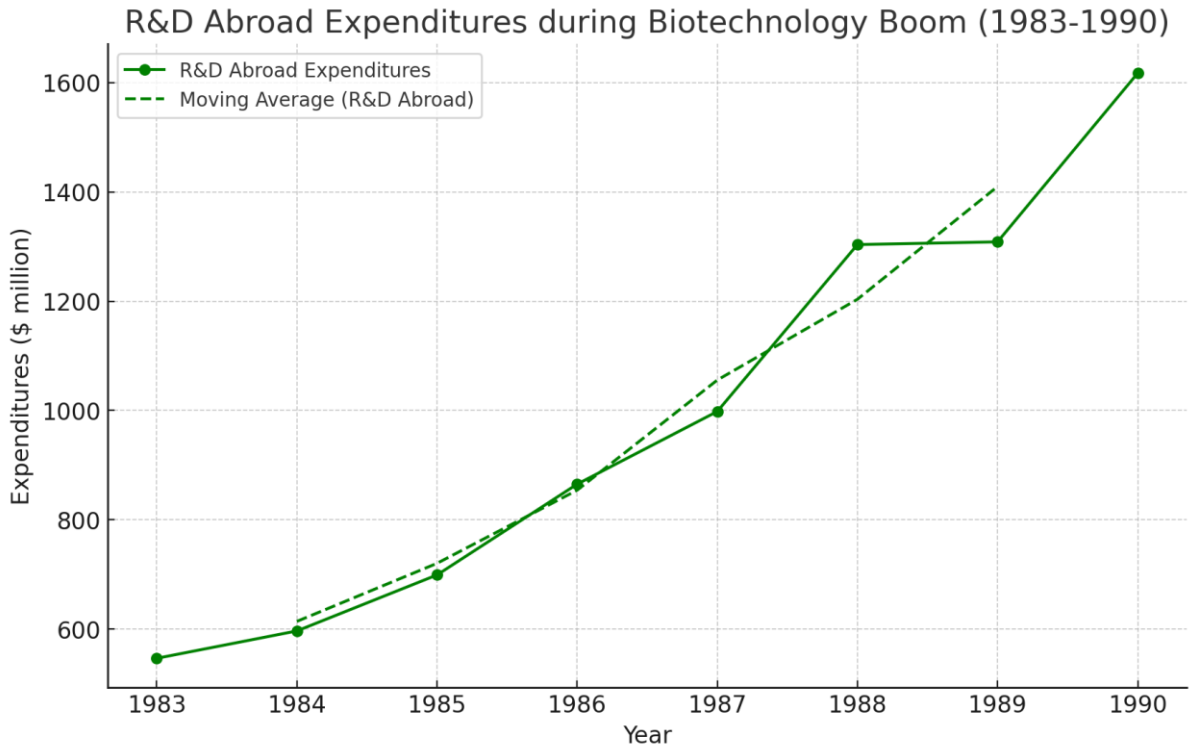
Graph 8. Total R&D Expenditures during the Biotechnology Boom by PhRMA Member Companies (1983-1990).

The graph representing Total R&D Expenditures during the Biotechnology Boom (1983-1990) shows a clear and uninterrupted upward trajectory. Over the period, R&D expenditures grew steadily from approximately $3200 million in 1983 to over $8400 million by 1990. This continuous increase reflects a phase of sustained growth in the biotechnology sector, driven by significant advances in genetic engineering, the development of recombinant DNA technology, and the commercialization of new biotech products. The overall trend indicates a strong commitment to R&D investments during this period, as companies and investors recognized the potential of biotechnology to revolutionize healthcare. Unlike other periods where peaks and troughs might indicate fluctuations in investment or responses to external factors**,** this graph suggests a period of confidence and consistent growth.



Graph 9. Domestic R&D Expenditures during the Biotechnology Boom by PhRMA Member Companies (1983-1990).

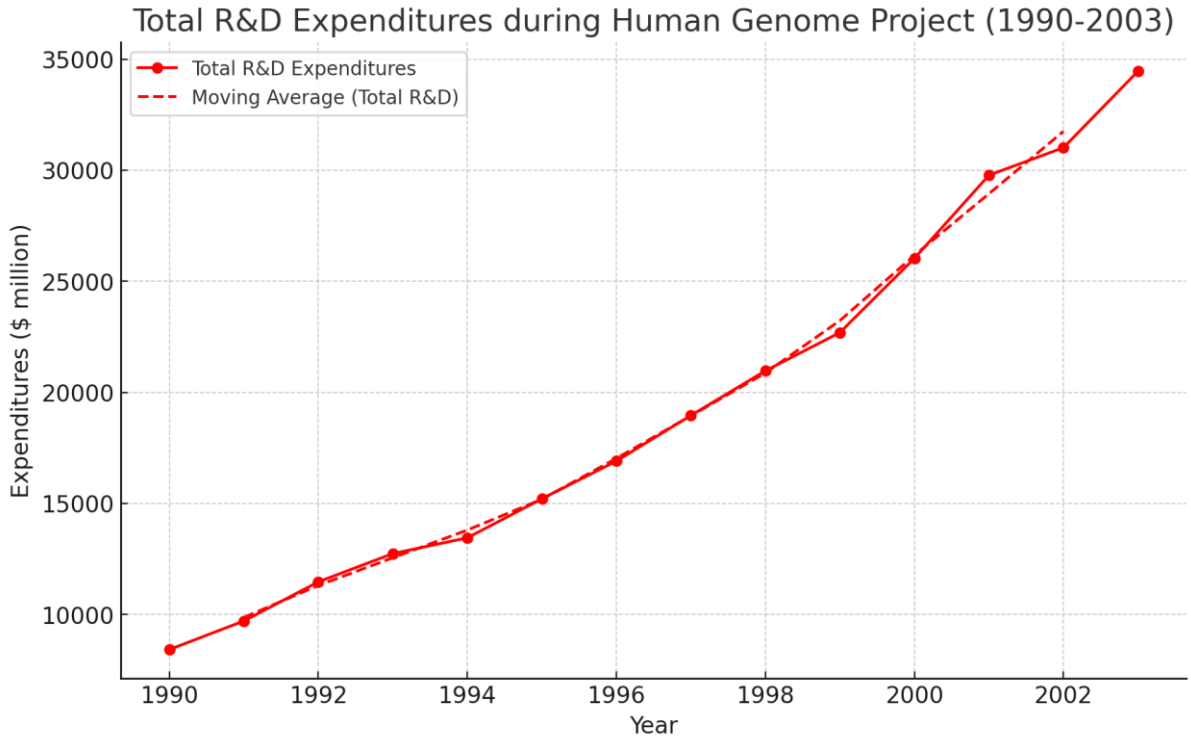
The graph representing Domestic R&D Expenditures during the Biotechnology Boom (1983-1990) displays a consistent upward trend, similar to the Total R&D Expenditures during this period. Domestic R&D expenditures grew from approximately $2500 million in 1983 to around $6800 million by 1990. However, unlike the total R&D graph, this graph shows a slight potential trough around 1988, where the growth rate temporarily slows before resuming its upward trajectory. The overall trend reflects robust and sustained investment in domestic R&D, driven by the rapid growth of biotechnology industry. The slight deceleration observed around 1988 could indicate a brief period of consolidation or strategic realignment within domestic pharmaceutical companies, possibly in response to early market feedback or evolving regulatory landscapes.



Graph 10. Abroad R&D Expenditures during the Biotechnology Boom by PhRMA Member Companies (1983-1990).

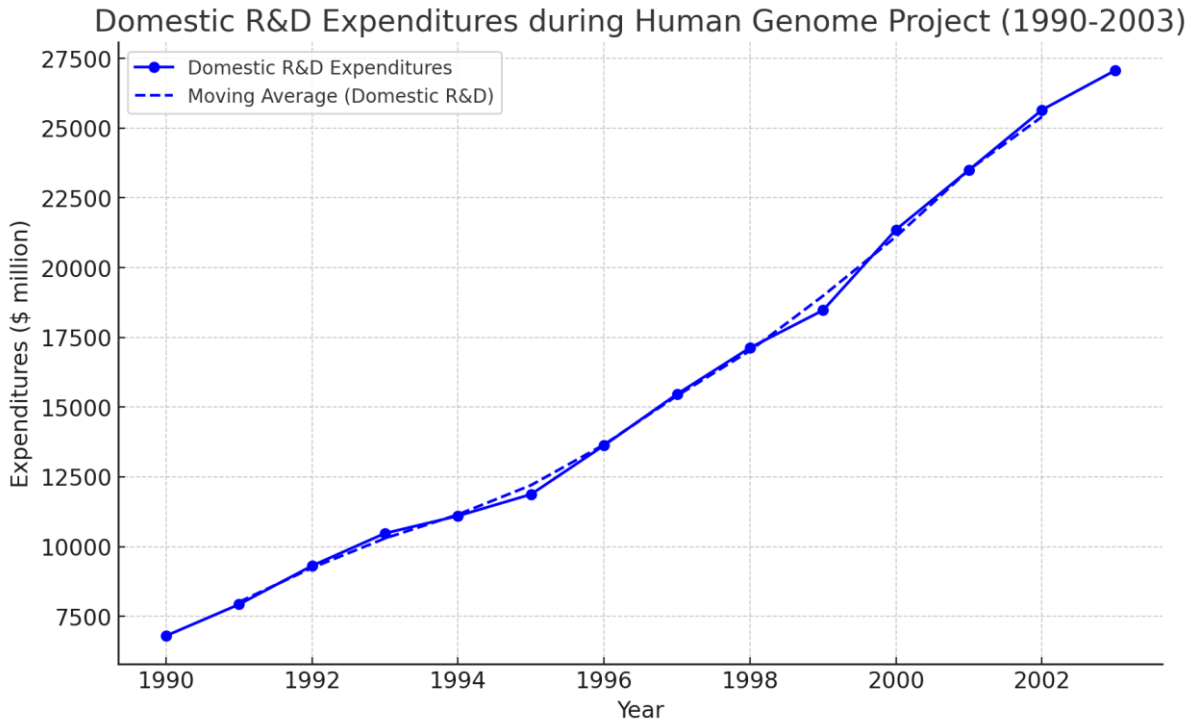
The graph representing R&D Abroad Expenditures during the Biotechnology Boom (1983-1990) shows a general upward trend, indicating a growing interest and investment in Abroad R&D efforts by pharmaceutical companies during this period. The expenditures grew from approximately $600 million in 1983 to over $1600 million by 1990. However, the graph also reveals some fluctuations, particularly around the years 1987, 1988, and 1989. The overall trend suggests that pharmaceutical companies were increasingly expanding their research efforts abroad, likely in search of new markets and innovative research opportunities. The increasing globalization of the pharmaceutical industry during this time is reflected in the steady growth of R&D expenditures abroad. There is a noticeable dip in the growth of R&D abroad expenditures around 1987. This could indicate a period where companies reassessed their international investments, possibly due to regulatory challenges, economic considerations, or strategic shifts in focus. Following the 1987 trough, there is a peak in 1988, where the expenditures saw a significant increase. This could reflect renewed confidence and reinvestment in international R&D projects, perhaps due to successful outcomes from previous initiatives or new opportunities in emerging markets. Another dip is observed in 1989, suggesting a possible reevaluation of international R&D strategies or the impact of external factors such as economic fluctuations or political instability.

4.2 Human Genome Project (1990-2003)



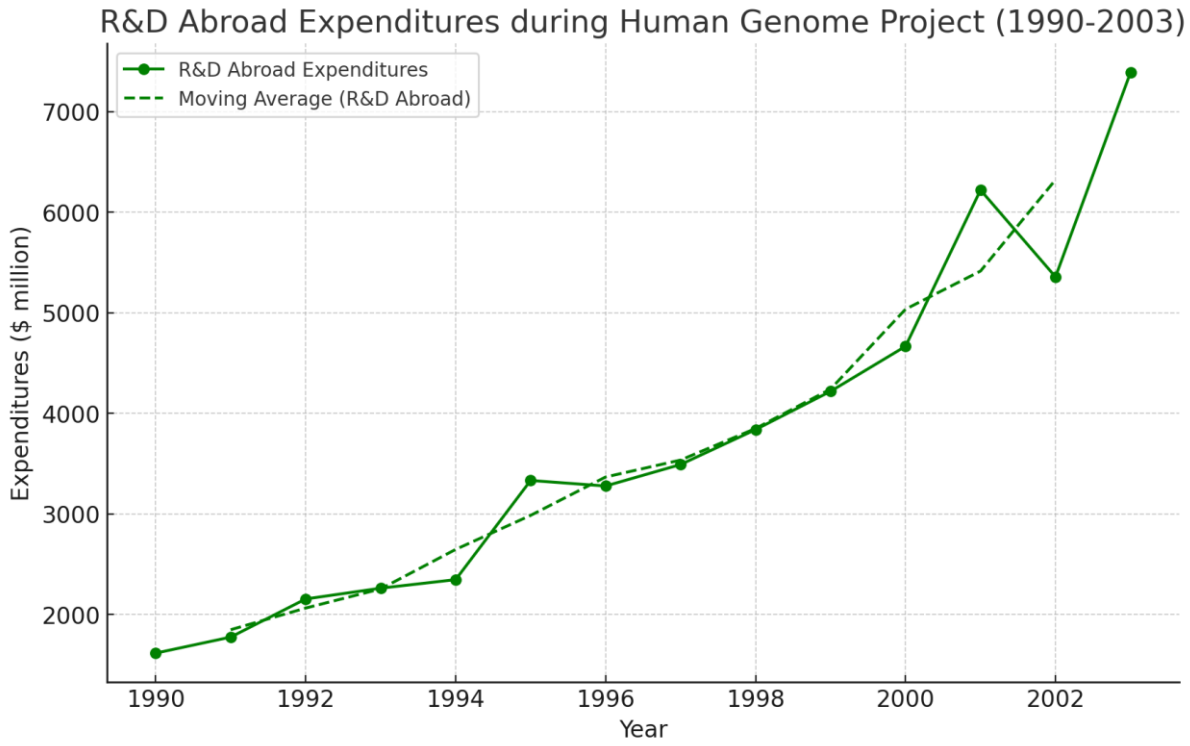
Graph 11. Total R&D Expenditures during the Human Genome Project by PhRMA Member Companies (1990-2003).

The graph that illustrates Total R&D Expenditures during the Human Genome Project (1990-2003) demonstrates a clear upward trend, signifying steady growth in R&D investments by PhRMA member companies. The total expenditures increased from around $8400 million in 1990 to over $34500 million by 2003, highlighting the significant influence of the Human Genome Project on the pharmaceutical industry's research priorities. Throughout the Human Genome Project, there was a sustained increase in R&D expenditures. This trend reflects the industry's growing focus on leveraging genomic data to drive drug discovery and the development of personalized therapies. The continuous growth in investment underscores the strategic importance placed on genomics by pharmaceutical companies during this era.



Graph 12. Domestic R&D Expenditures during the Human Genome Project by PhRMA Member Companies (1990-2003).

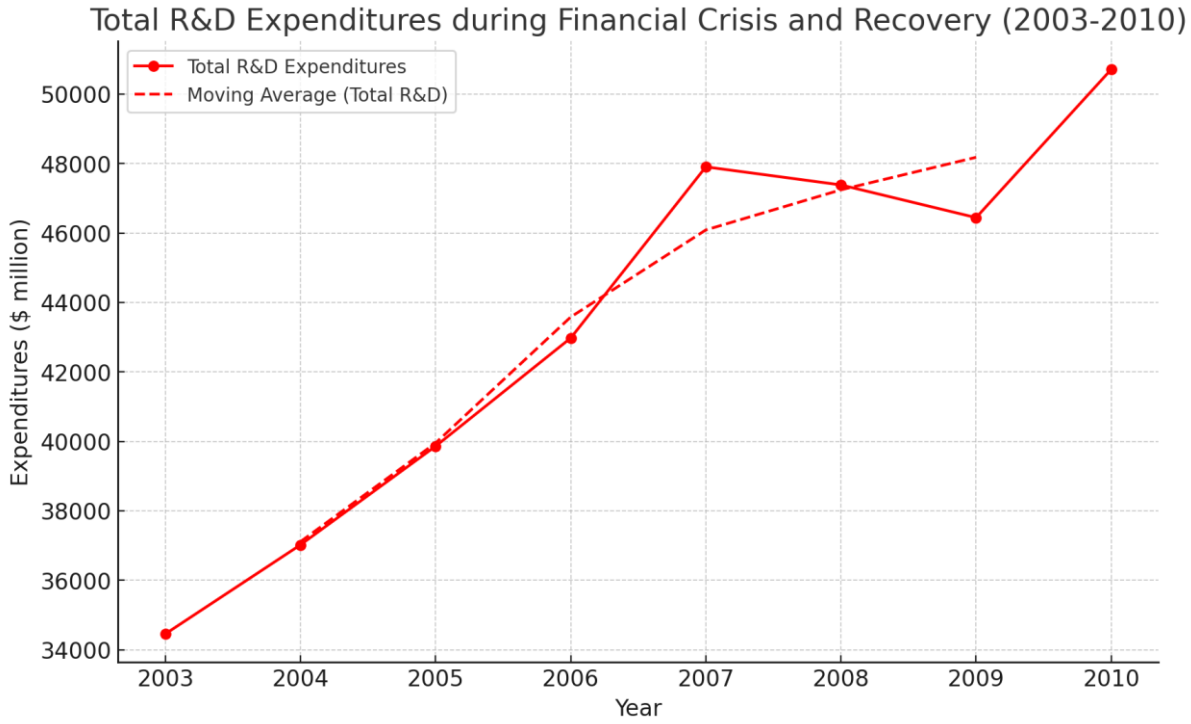
The graph illustrating Domestic R&D Expenditures during the Human Genome Project (1990-2003) showcases a steady and consistent upward trend, without any significant peaks or troughs. This suggests that the investment in domestic R&D by PhRMA member companies during this period was both stable and continuously growing. The graph reflects a sustained and uninterrupted increase in domestic R&D expenditures from approximately $6800 million in 1990 to nearly $27500 million by 2003.The smooth upward trajectory indicates that pharmaceutical companies consistently increased their investments in domestic R&D throughout the duration of the Human Genome Project. The steady increase in expenditures could be attributed to the progressive nature of genomic research, where consistent funding is required over an extended period to achieve meaningful results.



Graph 13. Abroad R&D Expenditures during the Human Genome Project by PhRMA Member Companies (1990-2003).

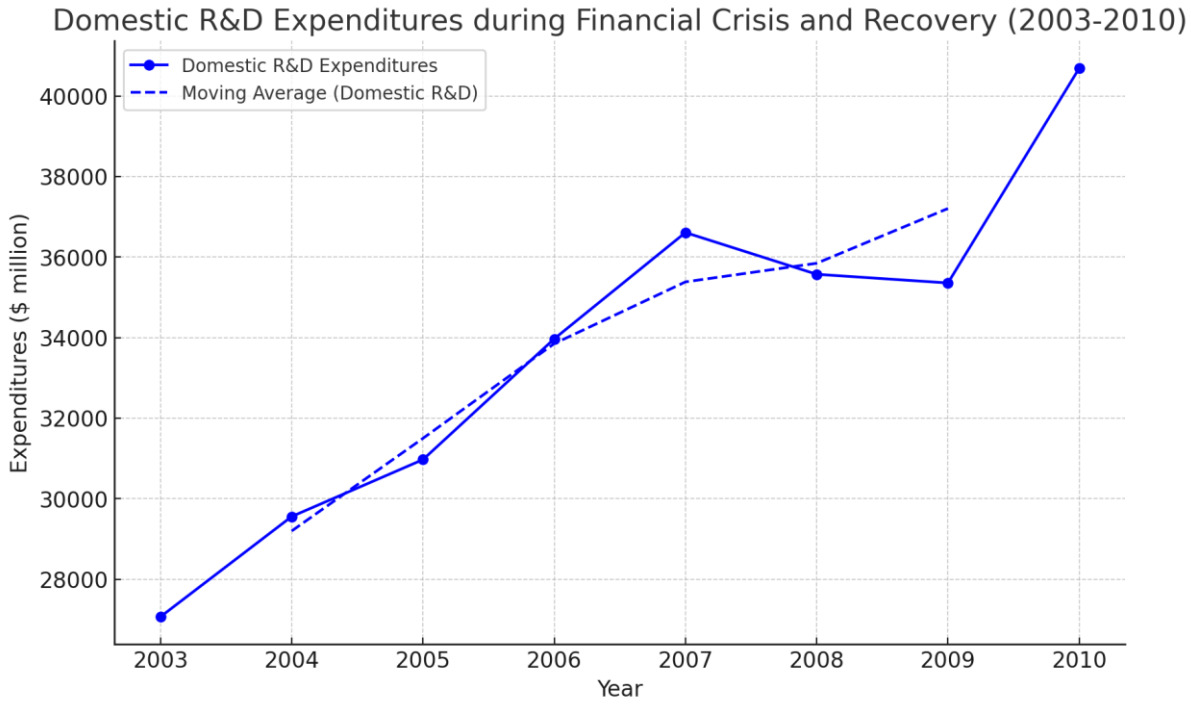
The graph representing R&D Abroad Expenditures during the Human Genome Project (1990-2003) demonstrates a more dynamic pattern compared to domestic expenditures, characterized by noticeable peaks and troughs. This variation suggests that international R&D investments were influenced by several external factors during this period. The overall trend shows an increase in R&D Abroad Expenditures from approximately $1600 million in 1990 to over $7400 million by 2003. Despite this overall growth, the graph displays several fluctuations, indicating periods of both accelerated investment and temporary pullbacks in international R&D. There is a visible through around 1994, where expenditures dipped before recovering in the following years. This could indicate a period of strategic reassessment or challenges in international markets that temporarily slowed down investment. A significant peak follows in 1995, suggesting a renewed surge in international R&D efforts, potentially driven by specific opportunities or successful risks abroad. Between 1996 and 1999, the graph shows relatively stable R&D expenditures with no major fluctuations, reflecting a period of steady but unremarkable growth. Another slight trough appears in 2000, hinting at possible economic or strategic factors that momentarily decreased R&D spending abroad. A prominent peak is observed in 2001, indicating a substantial increase in international R&D investments. This could be associated with specific advancements or the expansion of global R&D networks in response to new scientific opportunities from the Human Genome Project. Following this, there is a noticeable trough in 2002, suggesting a temporary reduction in spending, possibly due to external economic factors or strategic shifts.

4.3 Financial Crisis and Recovery (2003-2010)



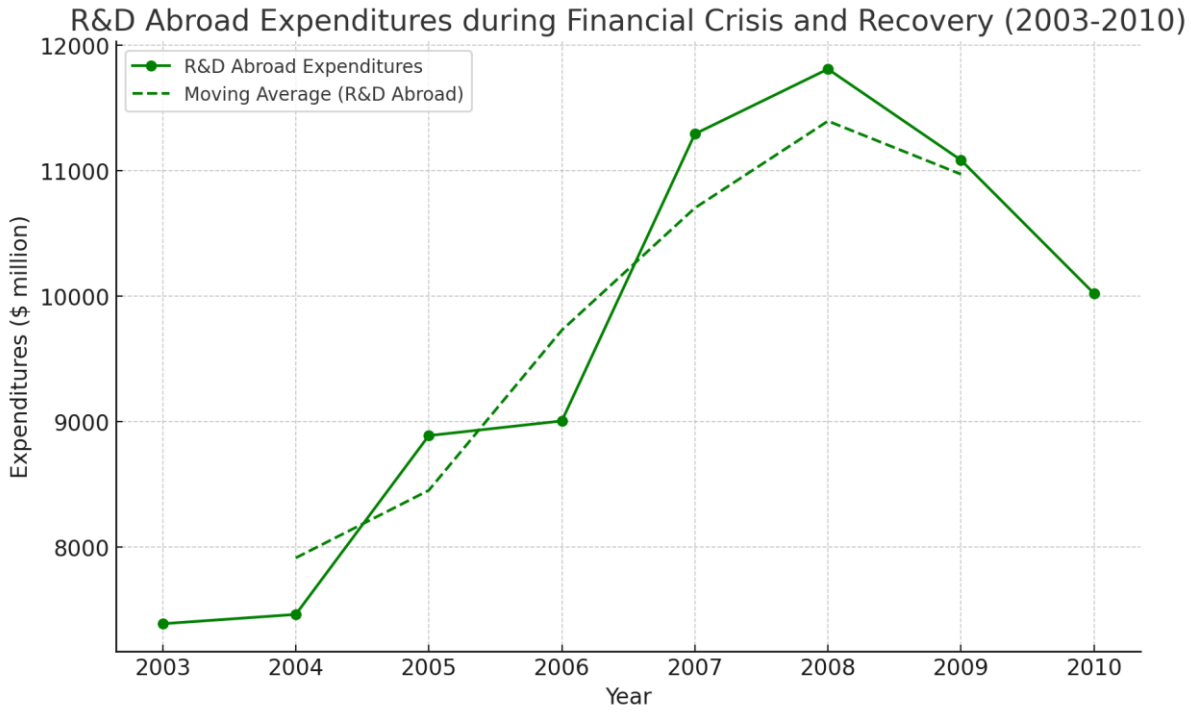
Graph 14. Total R&D Expenditures during the Financial Crisis and Recovery by PhRMA Member Companies (2003-2010).

The trend from 2003 to 2010 shows a general upward trajectory in total R&D expenditures, reflecting the industry's resilience and commitment to continued investment despite the economic challenges of the global financial crisis. Total R&D expenditures grew from approximately $34400 million in 2003 to around $50700 million by 2010. The graph shows a significant peak in 2007, indicating a strong investment in R&D during this period. This may be attributed to the momentum the industry had built before the crisis, with continued funding into promising areas of research. There is a noticeable trough in 2009, which likely reflects the impact of the financial crisis. Companies may have scaled back or reallocated R&D investments during this year due to economic pressures, uncertainty, and the need to conserve cash flows. The recovery is marked by a peak in 2010, suggesting that the industry rebounded relatively quickly. This peak could indicate renewed confidence and an increase in R&D spending as the global economy started to recover from the crisis. This analysis highlights how the pharmaceutical industry, particularly the companies within PhRMA, adapted to external economic shocks while maintaining a long-term focus on innovation and R&D investment.



Graph 15. Domestic R&D Expenditures during the Financial Crisis and Recovery by PhRMA Member Companies (2003-2010).

The graph of Domestic R&D Expenditures shows a general increase in investments from 2003 to 2010, reflecting the industry's ongoing commitment to research and development despite the global financial crisis. Domestic R&D expenditures grew from approximately $27000 million in 2003 to around $40700 million by 2010. Similar to the Total R&D Expenditures graph, the domestic R&D expenditures peaked in 2007. This suggests strong investment during this period, possibly driven by existing commitments to critical R&D projects and the momentum in the industry before the crisis hit. Domestic R&D was strong, driven by investments in new drug pipelines and technological advancements. Many pharmaceutical companies were expanding their drug pipelines, mainly focusing on discovering new drug targets and clinical trials. The driver for this is the need to replenish drug pipelines in anticipation of patent expirations on blockbuster drugs. One example is Pfizer, which made significant investments in its R&D pipeline, particularly in the areas of cardiovascular and oncology therapies, by 2007 over 212 active oncology studies, and moved more then 20% of its development budget to oncology. (24). There is a noticeable trough in 2009, indicating a dip in domestic R&D spending. This downturn can be directly associated with the financial crisis, as companies likely faced tighter budgets and had to make difficult decisions about which projects to continue funding. The graph shows a significant rebound with a peak in 2010, suggesting that domestic R&D investment recovered as the economy began to stabilize. This increase indicates renewed confidence and the resumption of deferred projects.

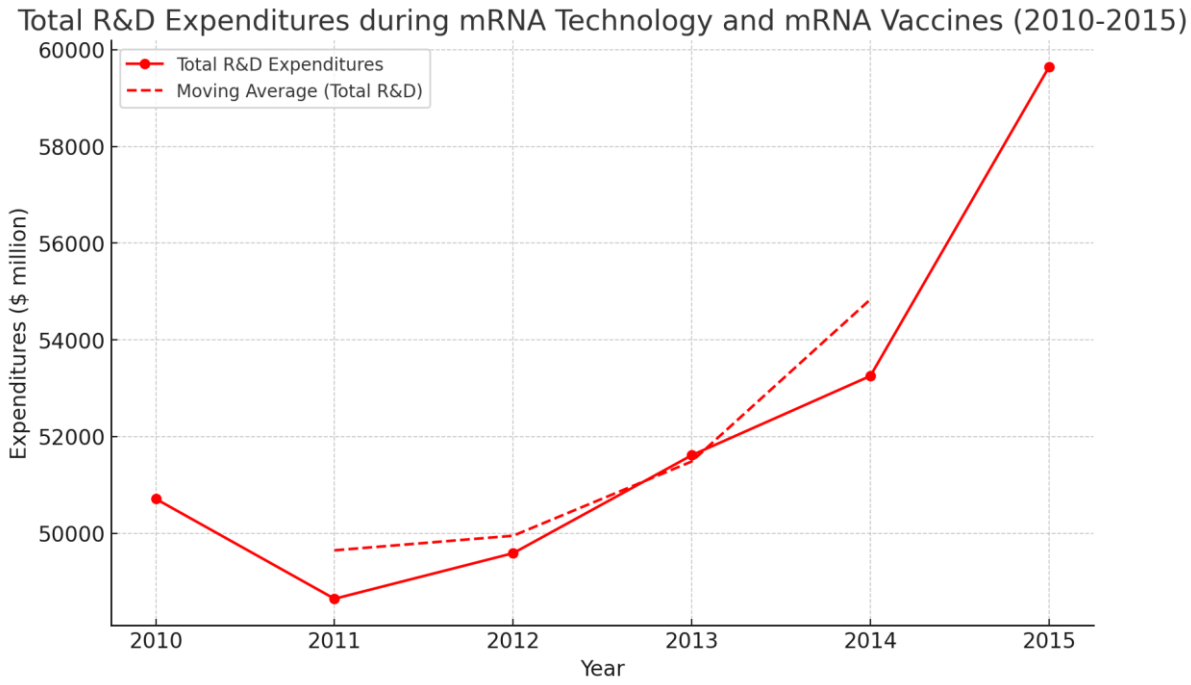


Graph 16. Abroad R&D Expenditures during the Financial Crisis and Recovery by PhRMA Member Companies (2003-2010).

During the period of the financial crisis and recovery (2003-2010), the trend in R&D abroad expenditures shows considerable fluctuations, reflecting the instability and economic uncertainty that characterized this time. Abroad R&D expenditures grew from approximately $7400 million in 2003 to around $10000 million by 2010 The overall trajectory is marked by a series of peaks and troughs, indicative of the global economic challenges faced by pharmaceutical companies. The graph indicates a significant trough in 2004. This decline could be attributed to the initial impact of the financial uncertainty, where companies likely reassessed and possibly reduced their international R&D investments due to the appearance of economic downturn. Following the trough in 2004, there was a marked recovery in 2005, as evidenced by the peak in expenditures. This could suggest that after initial caution, companies resumed their R&D activities abroad, perhaps driven by a need to sustain innovation pipelines and explore cost-effective research opportunities in foreign markets. A subsequent trough appears in 2006, showing another decline in expenditures. This downturn may indicate ongoing economic pressures or strategic realignments by companies to cope with the unfolding financial crisis. The expenditures reached two significant peaks in 2007 and 2008. The peak in 2007 might reflect a final push in R&D investments before the full effects of the financial crisis were felt. The 2008 peak, however, could represent the culmination of previously committed projects and investments before companies began to feel the severe economic constraints. Following the peaks, the graph shows a deep decline in expenditures in 2009 and 2010, reflecting the full impact of the global financial crisis. During these years, companies likely reduced or deferred

international R&D activities, focusing on conserving resources and stabilizing operations in a highly uncertain economic environment.

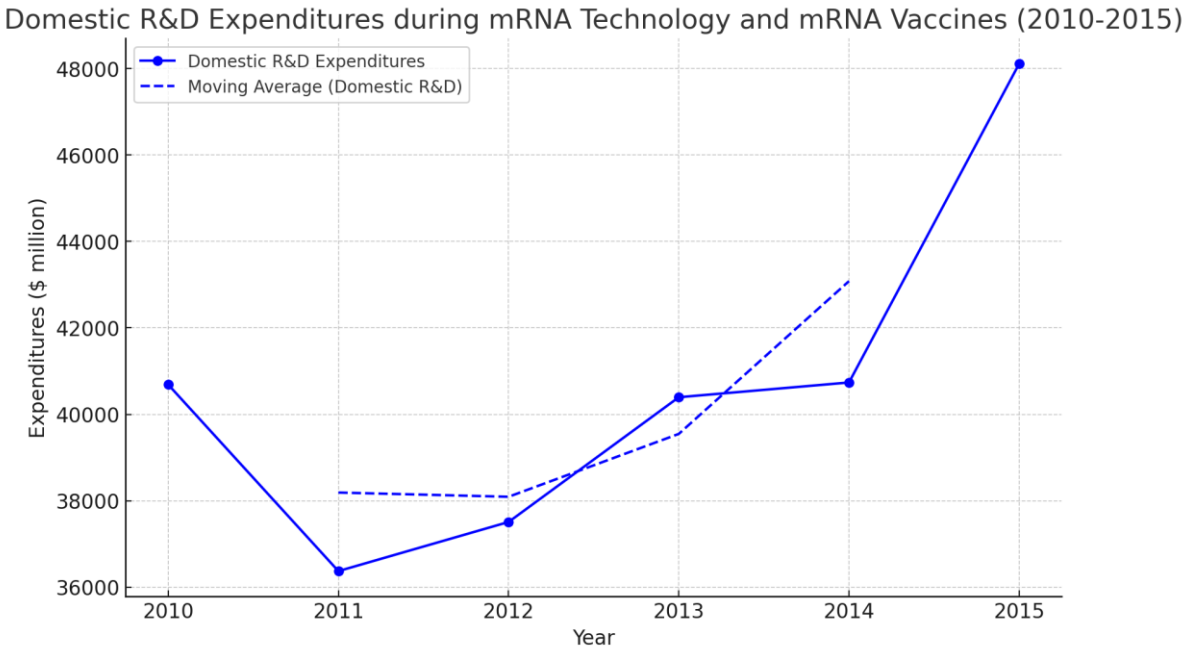
4.4 mRNA Technology and mRNA Vaccines (2010-2015)



Graph 17. Total R&D Expenditures during mRNA Technology and mRNA Vaccines by PhRMA Member Companies (2010-2015).

The period from 2010 to 2015, marked by significant advancements in RNA technology and mRNA vaccines, shows a distinct pattern in total R&D expenditures. Total R&D expenditures grew from approximately $50700 million in 2010 to around $59600 million by 2015. This era was characterized by the initial exploration and subsequent expansion of mRNA-based technologies, which would later become pivotal during the COVID-19 pandemic. The graph illustrates a generally upward trend in R&D spending, with notable fluctuations that align with key milestones in the development of these technologies. The graph shows a significant trough in 2011, indicating a temporary reduction in total R&D expenditures. This dip could be attributed to the early stages of investment in mRNA technology, where pharmaceutical companies were cautiously allocating resources towards what was still considered an emerging and experimental field. The industry might have been in a phase of evaluating the potential of mRNA technology, leading to a slower increase in spending. Another trough is observed in 2014, suggesting a period of reallocation or strategic reassessment of R&D investments. By this time, early successes in mRNA technology were becoming more apparent, but the industry may have been refining its focus, concentrating on the most promising avenues for development. The slight dip could reflect a temporary pause as companies optimized their R&D portfolios, possibly due to regulatory, technical, or financial considerations. The graph

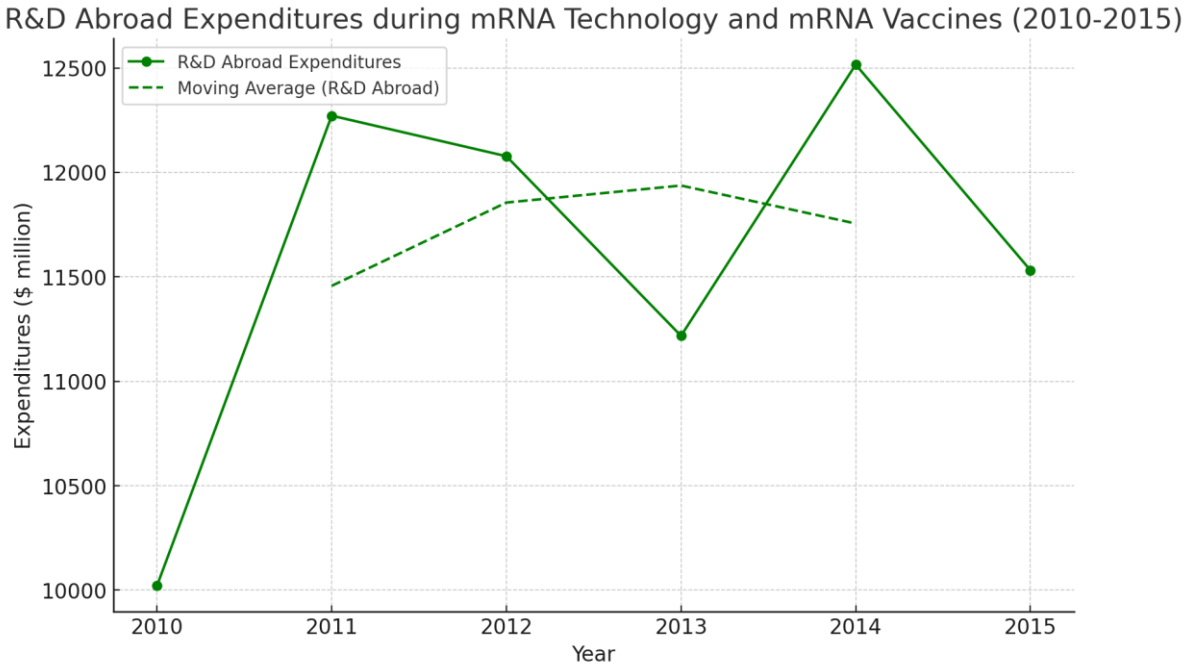
shows a sharp peak in 2015, indicating a substantial increase in total R&D expenditures. This peak likely represents a culmination of confidence in the mRNA platform, driven by promising early results and the anticipation of its potential in vaccine development. The significant rise in spending could also be linked to increased investment in late-stage development, preclinical trials, and the scaling up of production capacities, as the industry began to recognize the transformative potential of mRNA vaccines.



Graph 18. Domestic R&D Expenditures during mRNA Technology and mRNA Vaccines by PhRMA Member Companies (2010-2015).

The graph representing Domestic R&D Expenditures during the RNA Technology and mRNA Vaccines period (2010-2015) shows a distinct pattern of fluctuations with a general upward trajectory, particularly driven by companies like Moderna, which was established in 2010 with a focus on mRNA technology (25). Domestic R&D expenditures grew from approximately $40700 million in 2010 to around $48100 million by 2015 This period marked the early development phases of mRNA-based products, leading to a gradual but steady increase in domestic R&D spending This era captures the transition from early research and development in mRNA technologies to more robust investments as the potential of these technologies became clearer. The graph indicates a significant trough in 2011, showing a reduction in domestic R&D spending. This decline might reflect the initial uncertainty within the industry regarding the viability of mRNA technology, as companies cautiously allocated resources while evaluating the potential applications and challenges associated with this new platform. In 2012, the trough continues but with signs of recovery. This partial rebound suggests that while the industry was still cautious, there was a growing recognition of the need to invest in

mRNA research. The slight increase in expenditures could indicate the beginning of more focused efforts on specific mRNA-based projects. A peak is visible in 2013, where domestic R&D expenditures saw a noticeable increase. This peak likely corresponds to the successful outcomes of early-stage research, which provided the industry with confidence to accelerate investments in mRNA technology. The rise in spending may also reflect expanded research programs and early developmental trials. Following the 2013 peak, there is a slight downturn in 2014, indicating a temporary reduction in domestic R&D expenditures. This could be attributed to strategic reallocations of resources or the completion of certain early-stage projects. The industry may have been adjusting its focus, leading to a temporary dip in spending. The graph shows a substantial peak in 2015, signifying a significant increase in domestic R&D investments. This peak suggests a strong commitment from pharmaceutical companies to advance mRNA technology, likely driven by promising developments and the anticipation of broader applications, particularly in vaccine development. The spike in spending also reflects scaling up efforts as the industry prepared for more extensive clinical trials and potential commercial applications.

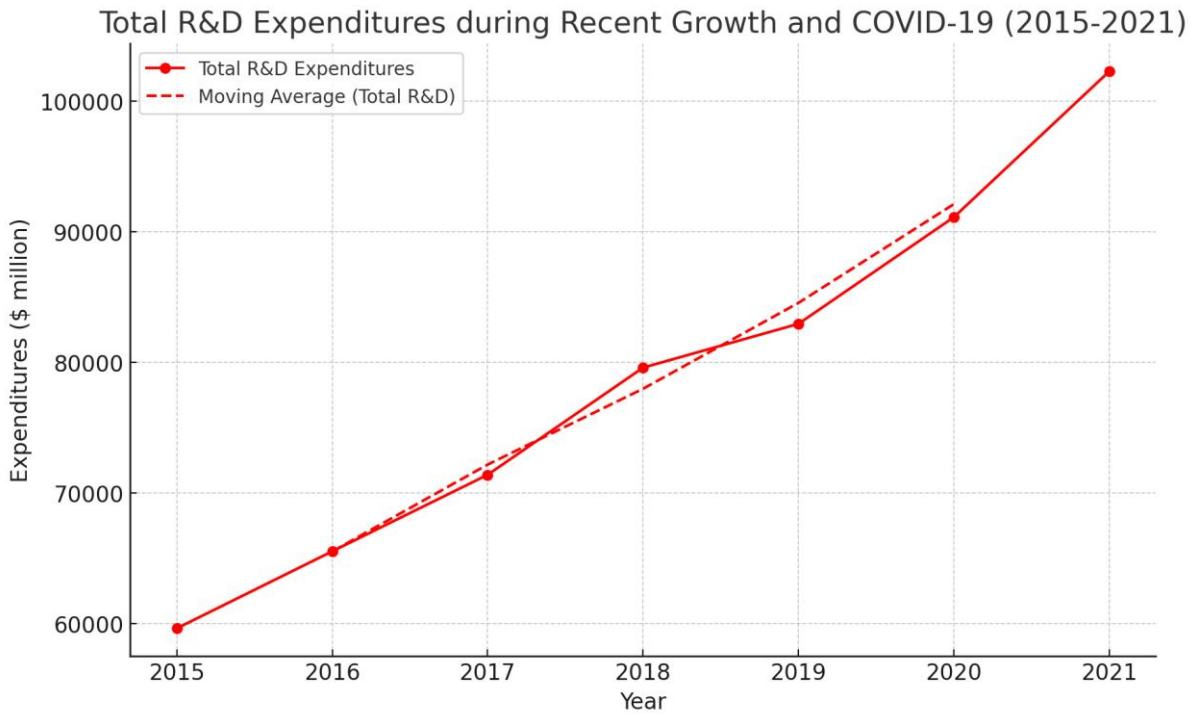


Graph 19. Abroad R&D Expenditures during mRNA Technology and mRNA Vaccines by PhRMA Member Companies (2010-2015).

The graph for R&D Abroad Expenditures during the RNA Technology and mRNA Vaccines period (2010-2015) exhibits significant volatility, reflecting the uncertainty and experimental nature of investments in emerging mRNA technologies. Abroad R&D expenditures grew from approximately $10000 million in 2010 to around $11500 million by 2015. The overall trend is less steady compared to domestic expenditures, indicating the cautious approach taken by international pharmaceutical companies during this period. The year 2010 starts with a

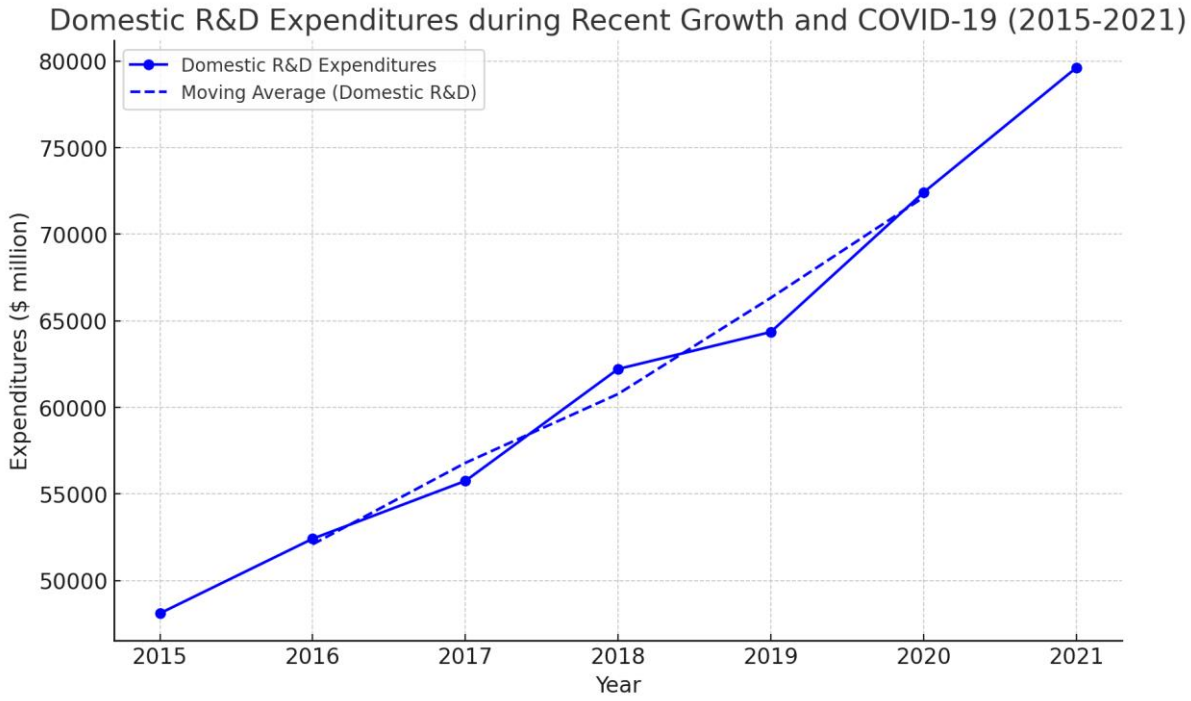
noticeable trough in R&D abroad expenditures. This low point could be due to the recent stage of mRNA technology, where international investments were still minimal as companies assessed the potential of this new platform. The hesitance to allocate large resources abroad likely reflects the global uncertainty regarding the viability of mRNA technology at this early stage. A sharp peak in 2011 follows the initial trough, indicating a sudden surge in investment. This significant increase suggests that early research and initial findings were promising enough to justify substantial international investment. Companies may have been expanding their R&D efforts abroad to leverage global expertise and resources in advancing mRNA technology. In 2012, the graph shows a smaller peak, suggesting a continuation of the momentum from 2011 but with a more measured approach. The reduced peak compared to 2011 could indicate that while investments continued, they were likely more targeted, focusing on specific areas of mRNA technology that showed the most promise. The graph dips again in 2013, marking another trough in R&D abroad expenditures. This decline might indicate a period of re-evaluation and consolidation, where companies slowed their spending to assess the progress made in previous years. The drop could also reflect strategic shifts in focus or delays in specific international projects. Another peak is observed in 2014, which suggests a renewed wave of confidence and investment in mRNA technology. This peak likely represents the ramping up of successful initiatives and the initiation of more advanced stages of development, possibly including larger-scale trials or broader collaborative efforts with international partners. The expenditures drop again in 2015, indicating a downturn following the 2014 peak. This final trough may represent the conclusion of some key international projects or a strategic pause as companies prepared to transition from R&D to commercialization, particularly with the promising developments leading to the later success of mRNA vaccines.

4.5 Recent Growth and COVID-19 (2015-2021)



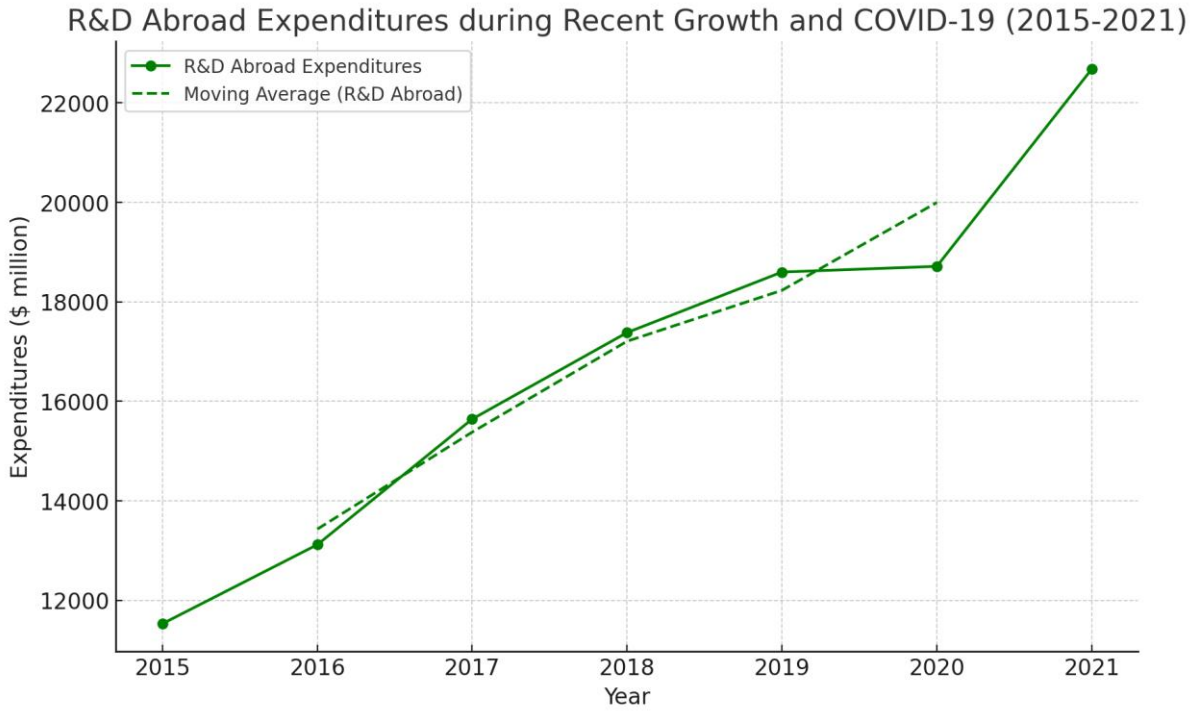
Graph 20. Total R&D Expenditures during Recent Growth and COVID-19 by PhRMA Member Companies (2015-2021).

The graph for Total R&D Expenditures during the Recent Growth and COVID-19 period (2015-2021) shows a consistent upward trend. Total R&D expenditures grew from approximately $50600 million in 2015 to around $102300 million by 2021 .This indicates a sustained increase in R&D investments by PhRMA member companies, particularly as the world approached and dealt with the COVID-19 pandemic. The overall trend is one of steady growth, reflecting the pharmaceutical industry's response to the growing demand for new therapies, vaccines, and treatments. Upon closer examination, there are no significant peaks or troughs in the total R&D expenditures during this period. The expenditures show a continuous rise, with minor fluctuations that do not amount to clearly defined peaks or troughs. This steady growth pattern suggests a period of strategic and consistent investment, particularly as the industry ramped up efforts in response to global health challenges. During this period, pharmaceutical companies likely adopted long-term strategies, focusing on scaling up R&D activities to meet the unprecedented global demand for new vaccines and treatments. The smooth upward trend suggests that these investments were well-planned and executed, without the need for changes or corrections.



Graph 21. Domestic R&D Expenditures during Recent Growth and COVID-19 by PhRMA Member Companies (2015-2021).

The Domestic R&D Expenditures graph for the period from 2015 to 2021 shows a consistent upward trajectory, indicative of sustained investment in domestic research and development by PhRMA member companies. Domestic R&D expenditures grew from approximately $48100 million in 2015 to around $79600 million by 2021 The growth is steady and reflects the increasing emphasis on developing new treatments and technologies, particularly in response to the COVID-19 pandemic. There are very subtle variations in the trend, but these are not significant enough to be classified as major peaks or troughs. The general upward movement suggests that any fluctuations were minor and likely part of normal annual variations in R&D spending. The sharp increase in spending towards 2021 corresponds with the pandemic response, highlighting a period of intensified R&D activity. However, the overall trend remains consistent without any sharp deviations.



Graph 22. Abroad R&D Expenditures during Recent Growth and COVID-19 by PhRMA Member Companies (2015-2021).

The R&D Abroad Expenditures graph for the period from 2015 to 2021 shows a steady upward trend, similar to the domestic and total R&D expenditures. Abroad R&D expenditures grew from approximately $11500 million in 2015 to around $22700 million by 2021 This indicates that PhRMA member companies consistently increased their investments in R&D activities abroad, reflecting a global approach to innovation and drug development. The graph shows a gradual increase during these years, however, the fluctuations are subtle and do not represent significant deviations from the overall trend. There is a noticeable trough in 2020, which likely corresponds to the initial impact of the COVID-19 pandemic. This dip could reflect temporary disruptions in global R&D activities due to lockdowns, supply chain interruptions, or reallocation of resources to immediate pandemic response efforts. The year 2021 shows a strong recovery, with a sharp increase in R&D expenditures abroad. This surge likely reflects the intensification of efforts to develop and distribute vaccines and other treatments globally, highlighting the importance of international collaboration during the pandemic.

5. Impact of External Factors on R&D Investments: A PEST Analysis

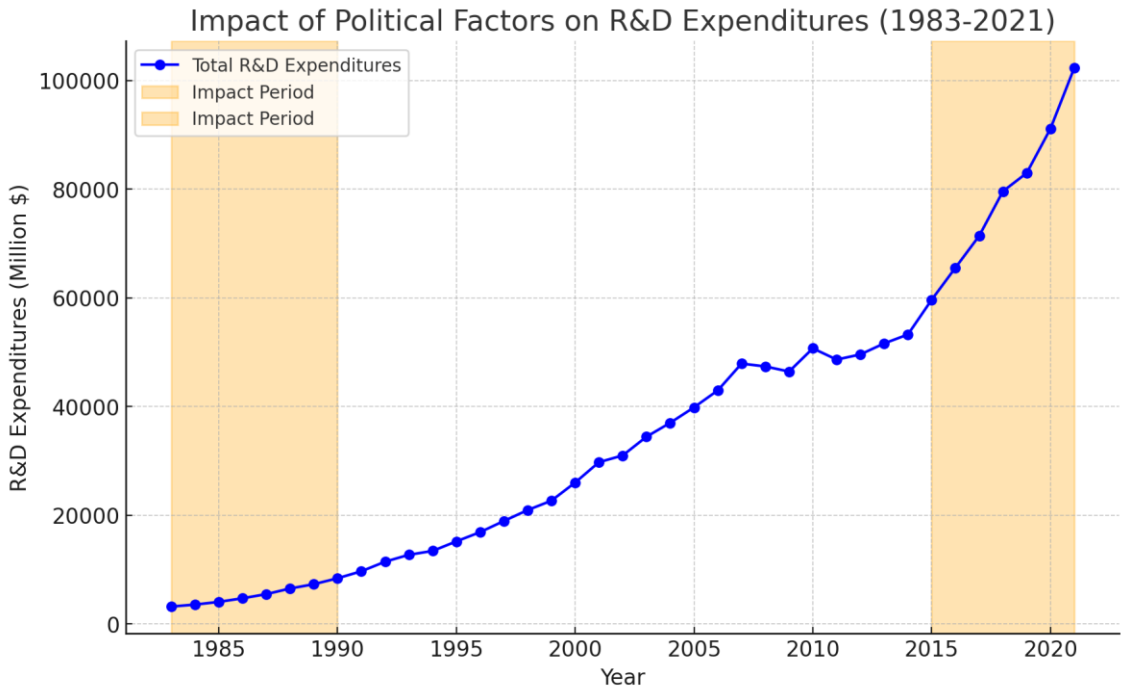
5.1 PEST Analysis Framework Overview

This section analyzes the impact of external Political, Economic, Social, and Technological (PEST) factors on pharmaceutical R&D expenditures from 1983 to 2021, considering their continuous presence throughout this period. By analyzing these factors in relation to key periods in the industry, we can better understand the forces driving R&D investment trends. This analysis is supported by graphical representations that highlight the impact of these factors over time.

5.2 Political Factors

Discussion

Political support, through government policies and regulatory frameworks, has been a significant driver of R&D expenditures. During the Biotechnology Boom (1983-1990), favorable policies such as the Orphan Drug Act and fast-tracked drug approvals spurred biotech innovation, leading to increased R&D spending. Similarly, during the COVID-19 pandemic (2015-2021), government initiatives and accelerated regulatory approvals facilitated a surge in R&D investments, particularly in vaccine development.

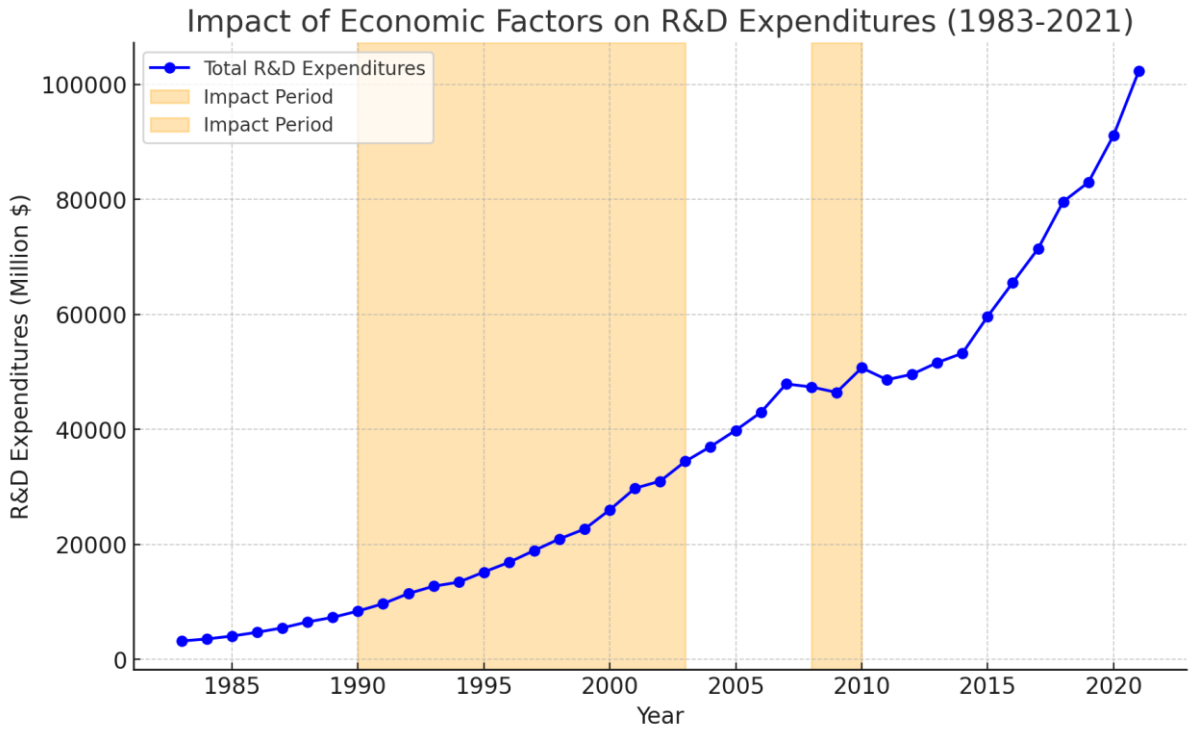


Graph 21. Impact of Political Factors on Total R&D Expenditures by PhRMA Member Companies (1983-2021). This graph illustrates the periods where political factors significantly influenced R&D expenditures. The orange-shaded areas represent time frames of strong political impact, such as during the Biotechnology Boom and the recent COVID-19 pandemic response.

5.3 Economic Factors

Discussion

Economic conditions have directly influenced R&D investments. The Human Genome Project era (1990-2003) benefited from economic prosperity, leading to substantial investments in genomics. Conversely, the Global Financial Crisis (2008-2010) saw a temporary dip in R&D expenditures as companies faced financial constraints. However, economic recovery efforts helped to restore R&D investments, highlighting the resilience of the pharmaceutical industry.

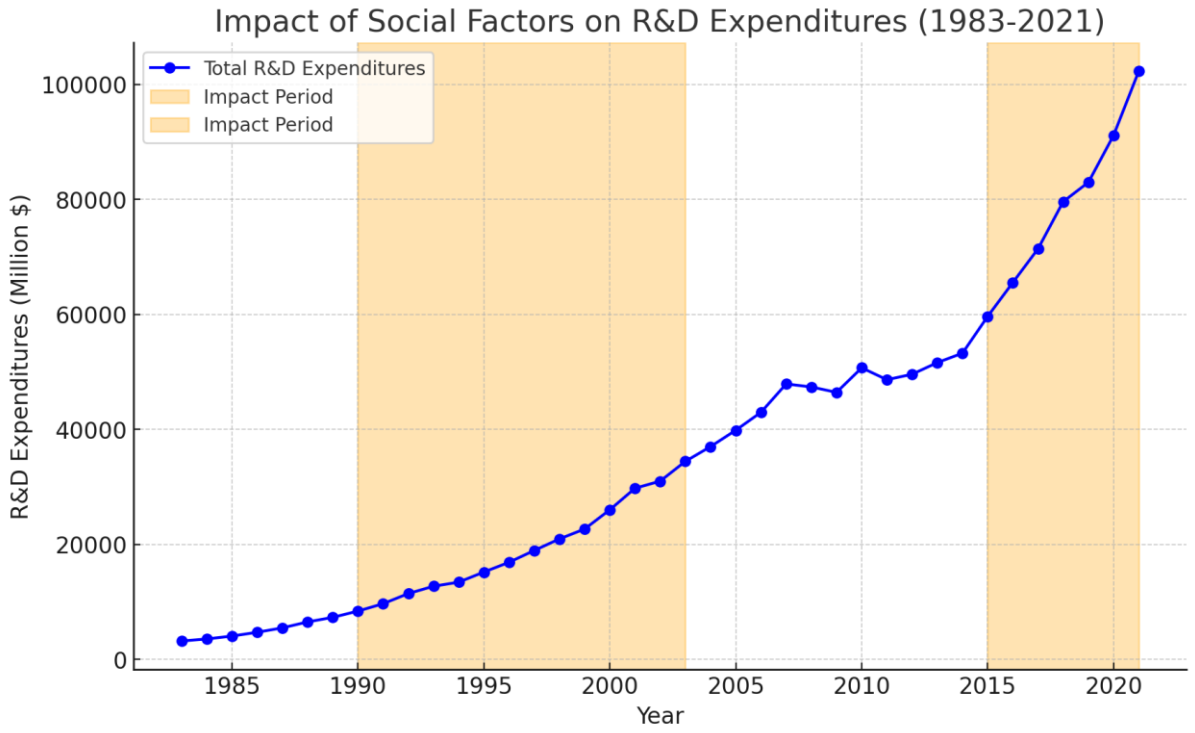


Graph 22. Impact of Economic Factors on Total R&D Expenditures by PhRMA Member Companies (1983-2021). This graph highlights the influence of economic factors on R&D expenditures. The orange-shaded areas correspond to periods of economic downturns and recoveries, such as the financial crisis of 2008.

5.4 Social Factors

Discussion

Social factors, such as public health awareness and demand for new therapies, have shaped R&D priorities. The Human Genome Project (1990-2003) was driven by societal interest in genetics and personalized medicine, leading to increased funding for related research. During the COVID-19 pandemic (2015-2021), the urgent need for vaccines and treatments drove unprecedented R&D spending, reflecting the direct impact of societal demands on the industry.

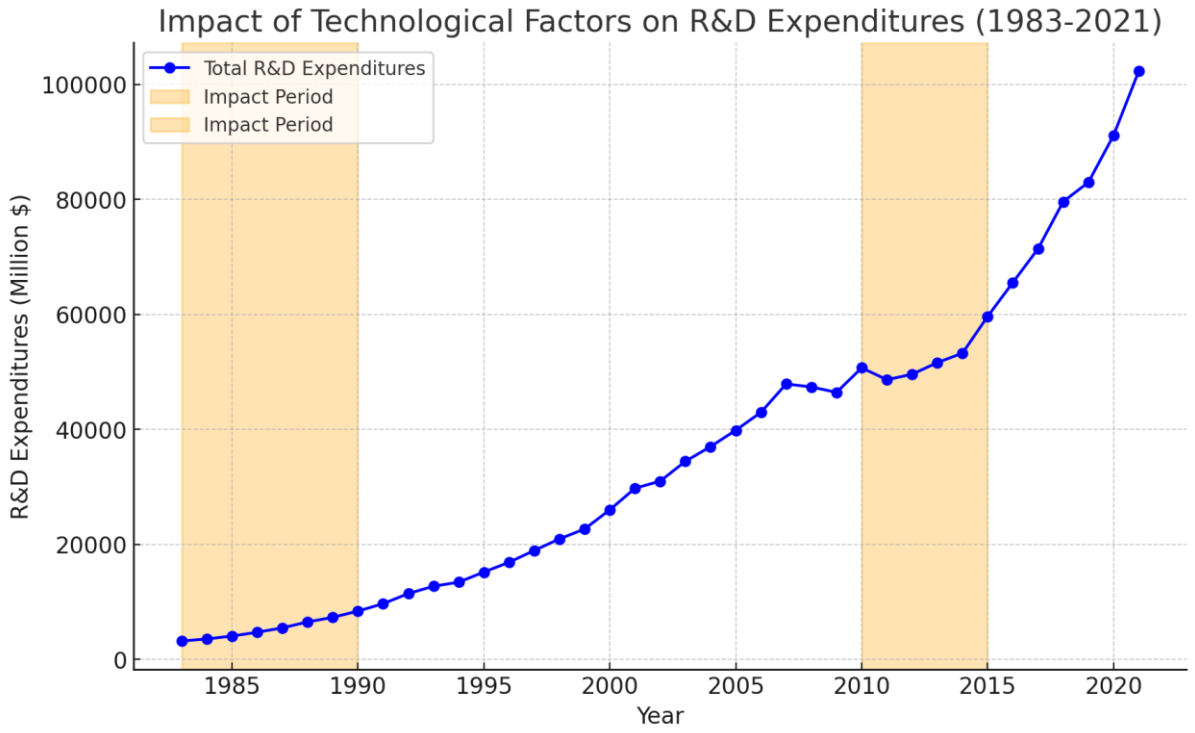


Graph 23. Impact of Social Factors on Total R&D Expenditures by PhRMA Member Companies (1983-2021). This graph shows the periods where social factors influenced R&D expenditures. The orange-shaded areas indicate times of heightened public interest in health and personalized medicine, such as during the Human Genome Project and the COVID-19 pandemic.

5.5 Technological Factors

Discussion

Technological advancements have been the most significant drivers of R&D growth. The Biotechnology Boom (1983-1990) was characterized by breakthroughs in genetic engineering, which fueled biotech innovation and increased R&D expenditures. More recently, the development of mRNA technology (2010-2015) laid the foundation for COVID-19 vaccines, underscoring the critical role of technological innovation in driving R&D investments.



Graph 24. Impact of Technological Factors on Total R&D Expenditures by PhRMA Member Companies (1983-2021).This graph illustrates the impact of technological advancements on R&D expenditures. The orange-shaded areas represent periods of significant technological innovation, such as the rise of mRNA technology.

6. Conclusion

As supported by the PEST analysis, the political, economic, social, and technological factors have significantly influenced pharmaceutical R&D expenditures from 1983 to 2021. Political support and regulatory changes were key drivers during pivotal periods, while economic conditions either driven or impaired R&D investments. Social demands, particularly for personalized medicine, guided R&D priorities, and technological advancements consistently fueled growth in spending. These insights highlight the importance of understanding external factors for guiding future R&D investments. Companies must be agile in adapting to political and regulatory shifts, ensure economic resilience during downturns, and align their R&D strategies with evolving social demands. Continued investment in new technologies is important to maintaining a competitive edge and driving future innovation. Ongoing political developments, economic changes, social shifts, and technological advancements will continue to shape R&D trends. Companies that anticipate and adapt to these factors will lead in the evolving pharmaceutical landscape. The dynamic of these PEST factors will be always relevant in defining the next wave of innovation and strategic decision-making in R&D. PEST analysis is a better method for this particular study because it provides better systematic, and long-term analysis of external factors that have influenced pharmaceutical R&D expenditures. Allows a comprehensive understanding of how the external environment has directioned industry trends over the nearly four-decade period, making it more suitable than SWOT for this type of historical and industry analysis. Given the evolving landscape of healthcare, it would be interesting to investigate the shifting focus of R&D investments between chronic diseases and infectious diseases. The pharmaceutical industry has allocated substantial resources to chronic diseases, driven by their prevalence and the long-term treatment needs that they create. However, the COVID-19 pandemic has highlighted the urgent necessity of being prepared for emerging infectious diseases. Understanding how R&D investments balance between these two areas could provide insights into how the industry can better prepare for future healthcare challenges. It could also guide strategic decisions in prioritizing investments based on evolving global health threats

7. References

1 - Ligon BL. Penicillin: its discovery and early development. Semin Pediatr Infect Dis. 2004 Jan 1;15(1):52–7.

2 - Son S, Lee K. Development of mRNA Vaccines/Therapeutics and Their Delivery System. Mol Cells. 2023 Jan 1;46(1):41–7.

3 - Pharmaceutical Research and Manufacturers of America. PhRMA Membership Survey 2022. Washington, DC: PhRMA; 2022 [cited 2024 May 12]. Available from: https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Refresh/Report-PDFs/P-R/PhRMA_membership-survey_2022_final.pdf

4 - Morgan S, Lopert R, Greyson D. Toward a definition of pharmaceutical innovation. Open Med. 2008;2(1)–e7.

5 - PhRMA. Home. PhRMA. [cited 2024 Apr 28]. Available from: https://phrma.org/

6 - Paul A. Offit MD. Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis. Yale University Press; 2008. 256 p.

7 - Tyrer L. Introduction of the pill and its impact. Contraception [Internet]. 1999 Jan 1 [cited 2024 Aug 25];59(1 SUPPL.):11S-16S. Available from: http://www.contraceptionjournal.org/article/S0010782498001310/fulltext

8 - Greene JA, Podolsky SH. Reform, Regulation, and Pharmaceuticals — The Kefauver–Harris Amendments at 50. New England Journal of Medicine. 2012 Oct 18;367(16):1481–3.

9 - Quianzon CC, Cheikh I. History of insulin. J Community Hosp Intern Med Perspect. 2012 Jan 16;2(2):18701. Available from: https://www.tandfonline.com/doi/full/10.3402/jchimp.v2i2.18701

10 - Peters C, Brown S. Antibody-drug conjugates as novel anti-cancer chemotherapeutics. Vol. 35, Bioscience Reports. Portland Press Ltd; 2015.

11 - Scheller EL, Krebsbach PH. Gene therapy: Design and prospects for craniofacial regeneration. Vol. 88, Journal of Dental Research. 2009. p. 585–96.

12 - National Human Genome Research Institute. Human Genome Project. National Institutes of Health. [cited 2024 Jun 17]. Available from: https://www.genome.gov/about-genomics/educational-resources/fact-sheets/human-genome-project

13 - Jim Zhang. Life Science Leader. 2009. The Impact Of The Financial Crisis On The Pharma And Biotech Industries.

14 - Wyke A, Mooney RW. The future of the life sciences industries: Aftermath of the global recession. 2010.

15 - National Library of Medicine. mRNA vaccines: MedlinePlus Genetics. MedlinePlus. [cited 2024 Jul 23]. Available from: https://medlineplus.gov/genetics/understanding/therapy/mrnavaccines/

16 - Killeen T, Kermer V, Troxler Saxer R. mRNA vaccine development during the COVID-19 pandemic: a retrospective review from the perspective of the Swiss affiliate of a global biopharmaceutical company. Vol. 16, Journal of Pharmaceutical Policy and Practice. BioMed Central Ltd; 2023.

17- Daems R, Maes E. The Race for COVID-19 Vaccines: Accelerating Innovation, Fair Allocation and Distribution. Vaccines (Basel). 2022 Sep 1;10(9).

18 - Haleem A, Javaid M, Singh RP, Suman R. Telemedicine for healthcare: Capabilities, features, barriers, and applications. Vol. 2, Sensors International. KeAi Communications Co.; 2021.

19 - Hammerstrom AE, Cauley DH, Atkinson BJ, Sharma P. Cancer immunotherapy: Sipuleucel-T and beyond. Vol. 31, Pharmacotherapy. 2011. p. 813–28.

20 - Mitra A, Barua A, Huang L, Ganguly S, Feng Q, He B. From bench to bedside: the history and progress of CAR T cell therapy. Vol. 14, Frontiers in Immunology. Frontiers Media S.A.; 2023.

21 - Fermaglich LJ, Miller KL. A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. Orphanet J Rare Dis. 2023 Dec 1;18(1).

22 - Kenton W. PEST analysis. Investopedia. 2024 [cited 2024 Jul 25]. Available from: https://www.investopedia.com/terms/p/pest-analysis.asp

23 - Investopedia. Compound Annual Growth Rate (CAGR). 2024 [cited 2024 Aug 10]. Available from: https://www.investopedia.com/terms/c/cagr.asp

24- Pfizer. Pfizer's growing strength in oncology. 2024 [cited 2024 May 16]. Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer_s_growing_strength_in_oncology

25 - Moderna. Our story. Moderna. [cited 2024 Aug 2]. Available from: https://www.modernatx.com/about-us/our-story

Annex 1: Evolution of R&D Expenditures: PhRMA Companies: Total, Domestic and Abroad (1983–2021)

(dollar figures in millions)

Year	Domestic R&D	Annual Percentage Change	R&D Abroad*	Annual Percentage Change	Total R&D	Annual Percentage Change
2021	$79,610.0	9.9%	$22,678.4	21.2%	$102,288.4	12.2%
2020	$72,412.1	12.5%	$18,714.2	0.6%	$91,126.3	9.8%
2019	$64,357.0	3.4%	$18,599.3	7.0%	$82,956.3	4.2%
2018	$62,219.7	11.6%	$17,383.1	11.1%	$79,602.8	11.5%
2017	$55,755.0	6.4%	$15,644.4	19.2%	$71,399.4	8.9%
2016	$52,418.2	9.0%	$13,120.1	13.8%	$65,538.3	9.9%
2015	$48,110.5	18.1%	$11,531.9	-7.9%	$59,642.4	12.0%
2014	$40,737.3	0.8%	$12,515.9	11.6%	$53,253.2	3.2%
2013	$40,396.0	7.7%	$11,217.6	-7.1%	$51,613.6	4.1%
2012	$37,510.2	3.1%	$12,077.4	-1.6%	$49,587.6	1.9%
2011	$36,373.6	-10.6%	$12,271.4	22.4%	$48,645.0	-4.1%
2010	$40,688.1	15.1%	$10,021.7	-9.6%	$50,709.8	9.2%
2009	$35,356.0	-0.6%	$11,085.6	-6.1%	$46,441.6	-2.0%
2008	$35,571.1	-2.8%	$11,812.0	4.6%	$47,383.1	-1.1%
2007	$36,608.4	7.8%	$11,294.8	25.4%	$47,903.1	11.5%
2006	$33,967.9	9.7%	$9,005.6	1.3%	$42,973.5	7.8%
2005	$30,969.0	4.8%	$8,888.9	19.1%	$39,857.9	7.7%
2004	$29,555.5	9.2%	$7,462.6	1.0%	$37,018.1	7.4%
2003	$27,064.9	5.5%	$7,388.4	37.9%	$34,453.3	11.1%
2002	$25,655.1	9.2%	$5,357.2	-13.9%	$31,012.2	4.2%
2001	$23,502.0	10.0%	$6,220.6	33.3%	$29,772.7	14.4%
2000	$21,363.7	15.7%	$4,667.1	10.6%	$26,030.8	14.7%
1999	$18,471.1	7.4%	$4,219.6	9.9%	$22,690.7	8.2%
1998	$17,127.9	11.0%	$3,839.0	9.9%	$20,966.9	10.8%
1997	$15,466.0	13.9%	$3,492.1	6.5%	$18,958.1	12.4%
1996	$13,627.1	14.8%	$3,278.5	-1.6%	$16,905.6	11.2%
1995	$11,874.0	7.0%	$3,333.5	***	$15,207.4	***
1994	$11,101.6	6.0%	$2,347.8	3.8%	$13,449.4	5.6%
1993	$10,477.1	12.5%	$2,262.9	5.0%	$12,740.0	11.1%
1992	$9,312.1	17.4%	$2,155.8	21.3%	$11,467.9	18.2%
1991	$7,928.6	16.5%	$1,776.8	9.9%	$9,705.4	15.3%
1990	$6,802.9	13.0%	$1,617.4	23.6%	$8,420.3	14.9%
1989	$6,021.4	15.0%	$1,308.6	0.4%	$7,330.0	12.1%
1988	$5,233.9	16.2%	$1,303.6	30.6%	$6,537.5	18.8%
1987	$4,504.1	16.2%	$998.1	15.4%	$5,502.2	16.1%
1986	$3,875.0	14.7%	$865.1	23.8%	$4,740.1	16.2%
1985	$3,378.7	13.3%	$698.9	17.2%	$4,077.6	13.9%
1984	$2,982.4	11.6%	$596.4	9.2%	$3,578.8	11.2%
1983	$2,671.3	17.7%	$546.3	8.2%	$3,217.6	16.0%
Average**		**10.4%**		**13.0%**		**10.6%**

* R&D Abroad includes expenditures outside the United States by U.S.-owned PhRMA member companies and R&D conducted abroad by the U.S. divisions of foreign-owned PhRMA member companies. R&D performed abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded.

** Average since 1970.

*** R&D Abroad affected by merger and acquisition activity.

Notes: All figures include company-financed R&D only. Total values may be affected by rounding.

Source: Pharmaceutical Research and Manufacturers of America, PhRMA Annual Membership Survey, 2022.