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Why is the pharmaceutical industry investing in targeted therapies? The emergence of "premium pharma"

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Abstract

Recent decades have witnessed a major transformation in biomedical knowledge production, framed as the rise of personalized, precision, or stratified medicine. While social scientists have explored the implications for disease classification, patienthood, datafication and governance, the central role of the

pharmaceutical industry in shaping this new biomedical paradigm remains under-examined. This paper addresses this gap by analyzing the industry's strategic shift since the 1990s from mass market "blockbuster" drugs to high-priced, targeted therapies for niche and stratified markets. Employing a mixed-methods approach-including regulatory data analysis, examination of industry business models and pipelines, and observation at international conferences-we chart the contours and drivers of this transition. Our findings reveal that targeted therapies, such as orphan drugs and precision cancer treatments, now dominate pharmaceutical pipelines, enabled by regulatory incentives (e.g., the Orphan Drug Act), expedited review pathways, and monopolistic practices like patent thickets and indication stacking. These therapies are cheaper to develop, yet command extremely high prices. We conceptualize this shift as the emergence of "premium pharma," a new sociotechnical regime characterized by intellectual monopoly capitalism, neoliberal deregulation, and financialization. Integrating Geels' Multi-Level Perspective with theories of intellectual monopoly, we identify a series of parallel regulatory, cognitive, and normative changes that have made this possible. We argue that premium pharma entrenches innovation for high-income markets and prioritizes rent extraction over public health, exacerbating global inequalities. This analysis offers a novel framework for understanding the political economy of contemporary biomedicine and its implications for therapeutic innovation and access.

Introduction

Major changes in the production of biomedical knowledge have been underway in recent decades. Social science scholarship has framed these as part of the shift to personalized, precision or stratified medicine driven by the development of genomics, a criticism of the limits of existing drug therapy and broader cultural and economic changes that value bespoke products and services. The focus of much of this work has been on changes in disease nosology (Green, Carusi et al. 2022), patienthood (Dam, Green et al. 2022), changing social relations (Prainsack 2018), datafication (Hoeyer 2019), regulation (Hogarth and Martin 2021) and future imaginaries (Tutton 2012). However, within this literature very little attention has been paid to the central role of the pharmaceutical industry in driving the emergence of this new type of biomedicine through the discovery, development and deployment of new therapies. It is no coincidence that an important part of the sector has undergone a transformative shift since the 1990s marked by a strategic pivot from mass-market "blockbuster" drugs to high-priced targeted therapies for niche and stratified markets. We will show how these products now constitute over 50% of all new drugs and a growing share of the industry's product pipeline.

This paper addresses this important gap in knowledge by charting the contours, dynamics, and political and economic drivers of these changes. Drawing on a mixed-methods analysis of regulatory data, industry business models and pipelines, and informed by observations at international conferences, we demonstrate how targeted therapies (e.g. orphan drugs, targeted cancer therapies) have become central to corporate strategies aimed at maximizing monopolistic rents through regulatory exclusivity and patent extensions. Key findings reveal that these products now dominate pharmaceutical pipelines, enabled by regulatory incentives such as the Orphan Drug Act. Targeted therapies are cheaper to develop than traditional drugs, make extensive use of expedited review pathways that lower evidential standards, and utilize monopolistic practices-including patent thickets and indication stacking. They have formed the

basis for very high prices, with the median US launch price for new cancer orphan drugs of ~ $300,000. We argue that this represents a transition to what we have called "premium pharma"- reflecting the emergence of a new sociotechnical regime underpinned by intellectual monopoly capitalism, neoliberal deregulation, and financialization. To clarify, our use of “premium pharma” is both heuristic and as a conceptual framework that can be operationalized and tested empirically. We present it here as a new concept, informed by empirical research, but do not hold it as a generalizable or ‘proven’ truth.

The paper uses a novel conceptual framework to understand this transition, by integrating Geels’ Multi-Level Perspective (MLP) - analysing meso-level regime changes in product development, business strategies, and regulatory rules - with theories of intellectual monopoly capitalism, which highlight how firms consolidate power through the control of intangible assets e.g. patents. In particular, the paper breaks new ground by demonstrating how the regulatory exclusivity granted by the 1983 US Orphan Drug Act has played a central role in furthering these intellectual monopolies across the world. The conclusion argues that premium pharma entrenches a regime where innovation is narrowly directed toward high-income markets, prioritizing rent extraction over public health needs. A major consequence of this is growing problems with access to these advanced therapies, especially in the Global South. By describing this systemic change and mapping these dynamics, the paper provides a new lens for understanding the powerful forces (re)shaping contemporary biomedicine and contributes to critical debates on therapeutic innovation and the political economy of global health.

Background

Before describing the key shifts in the pharmaceutical products and markets associated with targeted therapies, it is valuable to situate these within broader internal and external changes in the

pharmaceutical sector over the last 40 years. Internally, a series of important changes have occurred, including:

Scientific and technical innovation – new platforms and therapeutic modalities have been developed since the 1980s. These include novel biological drugs (therapeutic proteins, monoclonal antibodies, and cell and gene therapies), genomics and pharmacogenetics.

New imaginaries of personalized medicine – accompanying the rise of genomic technology has been the ability to stratify patient populations, enabling drug therapy to be targeted at disease sub-groups. This was bolstered by a growing critique of "one size fits all" therapy when it became clear that many patients failed to respond to treatment due to genetic differences (Hedgecoe and Martin 2003).

Decreasing productivity and difficulties sustaining the blockbuster business model – there has been a widely perceived "crisis" in the productivity of the global industry since at least the 1990s (Cockburn 2006). This has been marked by falling numbers of new drug products (until recently), despite a major increase in expenditure on research and development (R&D).

At the same time a number of important external financial, political, and regulatory pressures associated with the rise of neoliberal economics have come to bear on the pharmaceutical industry, resulting in significant structural change. These include:

Financialization - the pharmaceutical industry, in line with broader developments within the capitalist economy, has become highly financialized since the 1990s (Lazonick, Tulum et al. 2019). As a result, corporations have become increasingly influenced by financial institutions to prioritise shareholder value-creation and a shift towards the accumulation and management of intangible intellectual property (IP) assets, such as large patent estates, as a source of economic rents (Keenan, Monteath et al. 2023).

Globalization of intellectual property rights - the growing importance of IP assets to the pharmaceutical industry was greatly enabled by the 1995 Trade-Related Aspects of Intellectual Property Rights (TRIPS)

Agreement. It provided a minimum level of patent protection globally and obliged all countries to provide greater IP protection for pharmaceutical products.

Deregulation – a key tenet of neoliberal policies internationally from the 1980s onwards has been a push to lower the regulatory "burden" placed on industry by government. In relation to pharmaceuticals, this mainly involved a move towards a more permissive system for the approval and marketing authorisation of new medicines.

In response to both these external and internal changes, companies have searched for new products, markets and business models. They have adopted a number of strategies including: 1) much greater R&D outsourcing of drug discovery and development to small and medium-sized enterprises (SMEs) - especially in the biotechnology industry, which are now the source of most new medicines. 2) The rotation of product portfolios towards high-value secondary care markets based in hospitals, so that by 2022 more than 55% of US drug sales were for specialty products for the treatment of serious and often complex conditions, such as cancer, autoimmune and rare diseases (Biggs 2023). This has helped oncology to become by far the most important drug market. 3) The growth in biological drugs and complex advanced therapies (e.g. cell and gene therapies), which now constitute ~50% of the industry's new products. 4) A move from blockbuster products to so-called "nichebusters" aimed at smaller groups of patients mainly in secondary or tertiary care settings. This will be analysed in more detail below. However, the move to smaller specialist markets marks a major reorientation in the products made by the industry, the diseases targeted, and the business models used to sell them. The rest of the paper will analyse how such an important transformation came about, and the reasons for it. The paper does not seek to evaluate the considerable benefits some of these therapies offer to patients but rather understand how they became so important to the industry.

Conceptual framework

Conceptually this paper is situated within science and technology studies (STS), which sees technological innovation as not simply the unfolding of scientific progress guided by the hidden hand of the market, but rather a complex sociotechnical process (Callon 1999, MacKenzie and Wajcman 1999). Technologies succeed not simply because they are technically superior, but also because they can attract the support of multiple stakeholders involved in their development and use. The focus is therefore on the scientific, industrial, regulatory, clinical, policy, economic and social factors that enable successful adoption. In this way, new technologies are socially constructed through a process of co-production (Douglas 2012). In developing a framework for the analysis the paper draws on two intellectual traditions closely aligned with STS. Firstly, critical scholarship on the political economy of the pharmaceutical industry, and secondly, work in innovation studies that examines sociotechnical transitions and, in particular, Geel's Multi Level Perspective. This combination provides a novel framework for understanding both the nature of the changes underway and the forces driving these changes. It enables a consideration of how the industry's quest for monopoly over its markets has an impact on the structure and dynamics of the sector over time.

The political economy of the pharmaceutical industry

There have been a number of studies of the political economy of the pharmaceutical sector that examine the interplay between the political and economic power of the industry and how this shapes, and is shaped by, business strategies, state regulation and the structure of healthcare systems (Bourgeron and Geiger 2022, Kapczynski 2023, Roy 2023). At the heart of these discussions is understanding the way in which the power of the industry is built on its monopoly over the development, production and distribution of medicines and how this is embedded in multiple domains.

In theorizing this, the idea of Intellectual Monopoly Capitalism (IMC) is useful. This was first proposed by Pagano (2014) following the global TRIPs agreement. In elaborating this, there has been a focus on the

increasing role of intangible assets such as patents as a source of market power in global value chains (Durand and Milberg 2020). The making, trading and valorisation of different forms of assets (e.g. knowledge, technology, nature and infrastructures) has become an important strand of work in STS (Birch and Muniesa 2020). This pays attention to how assets have become the defining feature of technocapitalism and the way in which they generate future revenue streams (economic rents). Assetization underlies the shift from productive, commodity-based accumulation to rent-bearing property relations and involves enclosure (e.g., through IP rights), limiting access and generating monopoly profits for asset holders (Birch 2020).

In relation to pharmaceuticals, IMC has been elaborated by scholars in innovation studies who have looked at the strong correlation between patent portfolios and company profitability (Dosi, Marengo et al. 2023).

In her book *Capitalism, Power and Innovation,* Celia Rikap (2021) argues that dominant firms (e.g. Big Pharma) exercise control over knowledge and data to consolidate power, maximize economic rents, and perpetuate global inequality. This is achieved by privatizing knowledge and innovation networks through the creation of intangible assets, especially patents based on publicly funded research and open-source collaboration (ibid). It enables the widespread entrenchment of corporate power allowing monopolistic control over markets and gives priority to rent seeking over scientific and technical innovation. Monopoly power is maintained in a number of ways. Firstly, Rikap (2019) has shown how large companies act as “intellectual monopolies” to control critical IP and innovation hubs, whilst outsourcing peripheral R&D steps to universities and small firms.

Secondly, the monopoly power of large pharmaceutical companies increasingly rests on the intangible assets they hold, which include trademarks, trade secrets, brands, know-how etc. Of these, most attention has been given to the patents held on the drugs sold by firms which are the foundation for the industry’s very high rate of profit. A number of different strategies have been used by firms to maximise

returns from their patent estates and have been widely described and criticised in the literature. These include: a) aggressive litigation to defend key patents; b) the creation of patent thickets, where large numbers of related claims are made on a particular molecule or target to discourage competition (Gurgula 2017); c) “evergreening” where small alterations are made to a product to gain additional patent protection so that exclusivity can be extended (Hemphill and Sampat 2012, Annett 2021); d) “pay to delay” where following litigation with firms wanting to launch cheap generics, large companies settle the claim by paying these competitors to delay market entry so that monopolies can be extended (Feldman and Misra 2019).

Less attention has been given to how intellectual monopolies are created by, and maintained in, regulatory systems that control the licensing of pharmaceutical products. Important work in social science research has described how a more permissive regulatory framework has emerged since the 1980s particularly in the US (Abraham and Davis 2009) but the main focus here has been on the implications for public health, patient safety and evidential standards. The chief exception to this has been studies of the impact of orphan drug legislation, which will be discussed below. This paper will consider other ways in which regulatory exclusivity is created and extended by state agencies to further secure the monopoly rights of dominant companies as part of IMC.

Understanding sociotechnical transitions

The extent to which there is a sociotechnical transition within the pharmaceutical industry associated with the move to premium pharma is not assumed as a starting point for this paper. Instead, ideas taken from the Multi Level Perspective (MLP) of sociotechnical change (Geels 2002, Geels 2019) will be used as a heuristic tool to investigate the nature and extent of the changes underway. On the one hand, there are important shifts in the type of products being produced by the industry, the business strategies companies have adopted, the prices charged and the markets created. However, on the other hand, many of the same companies are involved and the fundamental economic, technological and political

relations between the key actors in the innovation system appear to be largely the same. As a consequence, rather than focusing on macro level "landscape" changes which appear to be limited, this paper will examine the meso level changes outlined above, in what Geels calls a sociotechnical regime (Geels and Schot 2007). These rules, institutions, infrastructures and practices structure sociotechnical systems and guide the actions of actors involved in innovation. The core elements of a sociotechnical regime include:

1) Networks of actors such as innovators, policymakers, suppliers, users, and financiers who work together to maintain the system's stability (e.g. collaborative research consortia).

2) Formal and Informal rules including cognitive rules, shared beliefs, problem-solving heuristics, and technical paradigms (e.g. ways of discovering new drugs).

3) Normative rules, such as cultural values, role expectations, and policy paradigms (e.g. expectations regarding personalized medicine).

4) Regulatory frameworks including laws, standards, and market regulations that legitimize certain technologies (e.g. drug approval regulations).

5) Material and technical components such as physical infrastructure, platforms and enabling technologies (e.g. novel therapeutic modalities).

An assessment of the extent to which these different elements are changing with the emergence of premium pharma will clarify the scope and significance of this shift. However, it must be stressed that this is not intended as a comprehensive evaluation of the overall process of sociotechnical change in this domain but rather is being used selectively as a starting point for further investigation.

Methods

This study integrates qualitative and quantitative analyses to examine meso level structural changes associated with the rise of the premium pharma regime.

The data for this paper were collected from multiple sources, including:

Overall problem framing – the idea that a major transition is under way in the pharmaceutical sector was developed and tested over the life of [project name redacted]. This involved attendance and ethnographic observations at >20 major scientific industry conferences on pricing, regulation and orphan drug development e.g. World EPA, World Orphan Drug Congresses (in Europe and USA), the RE(ACT) and IRDiRC Congresses, European Conference on Rare Diseases & Orphan Products), and NORD patient and patient forum.

Quantitative analysis of industry databases and publicly accessible data repositories. For the analysis of orphan drug approvals, data was collected from the public dataset of FDA Orphan Drug Designations and approvals (Search Orphan Drug Designations and Approvals) and European Commission Community Register of orphan medical products (Union Register of medicinal products - Public health - European Commission). We compiled data on orphan drug approvals granted by the FDA from 1983 to 2020, and by the EMA from 2000 to 2020. Multiple indications refer to approvals granted for distinct orphan designated indications of the same active substance. The industry product pipeline data were extracted from the Pharmaprojects database (Citeline) on 18 April 2024, using filters to include all pipeline drugs in Phases I, II, or III of clinical development. The dataset was further filtered by indication to identify those developed for rare diseases and then stratified to look at drugs targeting rare cancers. For analyses of drug prices and market size, we used public list prices and commercially available datasets (e.g. IQVIA). List prices reflect manufacturer-reported prices before confidential rebates, discounts, or negotiated agreements and may therefore overestimate actual transaction prices, which are not publicly

disclosed. Market size estimates derived from IQVIA data are subject to selection and measurement limitations because coverage can vary across products, firms, and regions, potentially biasing market-share comparisons.

While we analyse a premium pharma landscape characterised by high prices, strong market protection, and favourable regulatory environments, the ‘standard pharma’ model - including drugs developed for common diseases, generics, and off-patent brands, continue to operate outside this regime.

The shift to targeted therapies in the pharmaceutical industry

A working definition of targeted therapies

A number of terms are widely used to capture important changes in biomedicine over the last 20-30 years. These include personalized, precision, stratified and targeted medicine (Lesko 2007, Woodcock 2007, Tutton and Jamie 2013). It is beyond the scope of this paper to provide a detailed history of these terms and their usage, which has been extensively discussed elsewhere (Redekop and Mladsi 2013). It is, however, worth noting that the idea of personalized medicine has a broad cultural salience, evoking notions of treatment tailored to a specific individual. Whilst there are a small number of therapies that are designed with this in mind (e.g. autologous cell therapy), this is not an accurate description of most of the products manufactured by the pharmaceutical industry that have been labelled as personalized medicine. Similarly, the idea of precision medicine, which moves away from the notion of individualized treatment (Au 2021), also does a lot of normative work by implying a level of accuracy in treating a disease that is rare in pharmacology. Instead, the term ‘targeted therapy’ will be used in this paper as it provides a tighter definition that can be more easily operationalized.

Specifically, we adopt a market-based definition where targeted therapy refers to products developed for niche or segmented markets in contrast to drugs aimed at undifferentiated mass markets. A niche market

is a small and specialized part of a larger market, and the idea of segmentation refers to the division of customers (i.e. patients) within the broader market into sub-groups.

There are two types of targeted therapies that will be discussed here. Firstly, drugs aimed at very small, rare disease markets and specifically so-called orphan drugs defined by the US Orphan Drug Act (ODA, 1983) and similar regulations in many other countries. This legislation was introduced to address the shortage of medicines for rare diseases due to market failure and provided significant commercial incentives for companies to invest in this area. These included seven years of market exclusivity for orphan designated products, tax credits and fee waivers. Under the ODA, drugs are designated as having orphan status if the disease affects less than 200,000 people in the US. The ODA has been highly successful in incentivising commercial investment in rare diseases (see below). In this way a regulatory category establishes a niche pharmaceutical market. It should also be noted that these rare disease categories have historically been defined using clinical symptoms combined with specific diagnostic tests but are increasingly constructed using genomics and other molecular biomarkers.

Secondly, the term targeted therapy is most commonly used to describe oncology drugs that are directed at particular molecules (drug targets) associated with various forms of cancer. Such targeted therapies are defined by having a molecular target specified in their regulatory approval rather than simply treating a clinically bounded disease category. This may be done in several ways, including specifying a molecular drug receptor or defining a disease category using one or more qualified (i.e. approved) molecular biomarkers. In this way a regulatory body enables an established clinical category to be reconstructed in molecular terms, often redrawing its boundaries and breaking a single disease entity (e.g. breast cancer) into a series of smaller disease sub-sets (segments). Regulators, such as the FDA, are increasingly involved in validating the biomarkers that define disease categories used in the approval process. Whilst this sort of targeted therapy is being developed in many disease areas, it is dominated by rare oncological drugs.

Both orphan and targeted cancer drugs are therefore aimed at specific disease populations that are embedded in the regulatory process of approving a new medicine. As a consequence, targeted therapies are a regulatory construct. The increasing use of a molecular nosology and biomarkers is being supported by many national and regional regulators, but it is the US FDA that has played the leading role in the development of targeted therapy.

A changing market: from "blockbusters" to "niche-busters"?

The development of targeted therapies must be placed in the context of longer term shifts in the pharmaceutical marketplace, most notably the changing importance of blockbuster drugs aimed at large mass markets and with sales >$1Bn a year. These blockbuster products increased rapidly at the end of the 1990s from a low base that made up <10% of global sales in the 1980s, so that between 1997-2006 the number of blockbusters grew from six to 52 (Aitken, Berndt et al. 2008). Their proportion of global sales also increased from 12% in 1996 to ~50% by 2006. However, a number of key patent expiries meant that both the number of blockbusters and their sales fell rapidly after this peak (Collier 2011). This decline was exacerbated by a slowdown in US drug expenditure and rapidly increasing generic sales, and prompted debate over the development of new business strategies based on so called "nichebusters" aimed at much smaller market segments (Dolgin 2010, Marselis and Hordijk 2020).

Several drugs and companies demonstrated the commercial viability of products for niche or segmented markets during this period each gaining blockbuster sales of >$1Bn (Meekings, Williams et al. 2012). The number of companies developing orphan drugs and/ or targeted cancer therapies grew steadily after 2010. In the case of orphan drugs there was a major increase in the involvement of large companies, especially after 2015 (author paper under review). One consequence of the success of these targeted therapies was that they increasingly had sales of over $1Bn, blurring the distinction between blockbusters and nichebusters. As many as 50% of new blockbuster products are now targeted therapies. The total number of blockbuster products stabilized after the financial crisis of 2007/8 accounting for between 30-

40% of global sales but this increased after 2018. It is striking that as many as 70% of these blockbusters are “me too” drugs, variants of established products that only offer incremental improvement on the original medicine (Schuhmacher, Hinder et al. 2022). The continuing reliance of the industry on this small group of best selling medicines is shown by the fact that between 2012-22 the top 20 companies launched 36 blockbusters representing 70% of total sales by new drug launches.

However, recent analysis of new FDA drug approvals found that whilst there are a record number of new drugs reaching the market, it is estimated that the peak sales of these products will only be ~50% of the long-term average and as few as 24% will become blockbusters (Baedeker, Ringel et al. 2023). Furthermore, of the 15 oncology drugs approved in 2023 only two are likely to gain blockbuster sales, highlighting a shift towards drugs targeted at smaller stratified patient populations (ibid). It therefore appears that whilst the blockbuster model has been central to the financial success of the industry, an increasing proportion of these products are targeted therapies. Going forward there may be more products but with lower sales reflecting the process of market segmentation. This points to an important historic shift in the sociotechnical regime (see analysis of MLP in Table 2), with companies adopting novel business models and targeting new products and markets.

The growth of targeted therapies

Despite being developed for rare diseases only affecting very small patient populations the incentives provided by orphan regulations have led to a massive growth in the number of new orphan approvals. Graph 1 shows FDA approvals increased from less than 10 a year in the early 1980s to around 80 a year by 2000, although this growth was less marked at the EMA. It is also striking that between 2019-24 over 50% of all new drugs (molecules) approved by the FDA had orphan status (FDA 2025). This is a remarkable shift in the products developed by the industry, and by 2022 some 880 orphan drug approvals had been granted by the FDA for use in 390 rare diseases, although much of this was focused on rare cancers (Fermaglich and Miller 2023).

Graph 1: Growth in annual orphan approvals by FDA and EMA (1983-2020)

The global market for orphan drugs was estimated to be worth $193Bn in 2024, an increase of nearly 25% from 2022 and was projected to have a compound annual growth rate (CAGR) of ~12% (Precedence Research 2025). Orphan drugs were also estimated to compose 20% of the global drug market, with this expected to rise slightly over the next decade.

There has also been a similar large increase in the number of targeted cancer drugs. Between January 2000-October 2022 573 agents were approved by the FDA for oncology indications. Of these, 48% were targeted small molecule drugs, 43% were biologicals, most of which were targeted, whilst conventional cytotoxic therapies made up only 9% (Hilas 2023). The use of biomarkers in these approvals increased from 32% between 2000-04, to 43% between 2020-22 (ibid). Market research studies estimate that by 2024 targeted therapies accounted for some 59% of the anti-cancer drug market with sales of $80Bn and a compound annual growth rate of ~7% (Fact.MR 2025).

The future is targeted

As of mid-2024, a total of 8,477 drugs were in the global industry clinical development pipeline (i.e. in Phases I–III), according to Citeline's Pharmaprojects database, with 44% in Phase I, 41% in Phase II, and 15% in Phase III. A substantial portion of the pipeline (41%, 3,436 drugs) were for rare diseases, and within this subset, over half (1,932 drugs = 23% of total) were focused on rare cancers. In terms of therapeutic areas, oncology dominated the global pipeline with 3,495 (41%) of all drugs, followed by neurological (1,333 = 18%) and alimentary/metabolic indications (1,189 = 14%), underscoring the continued priority given to cancer drug development across both common and rare indications. In fact,

rare cancer drugs constituted the single largest category, greater than for non-cancer rare diseases (21%) and non-rare cancer drugs (18%). If we aggregate the figures for rare diseases and anti-cancer agents in development and take into account the overlap in the rare cancer area and assume that 60% of non-rare cancer therapies are targeted (see above), then more than 50% of all therapies in global clinical development are targeted according to the definition used here.

In summary, this section has charted a broad shift in the types of products being developed by the pharmaceutical industry, which increasingly target small niche (orphan drug) or segmented (oncology) markets. These areas have grown rapidly and are now amongst the most important parts of the global market, as reflected by both current sales and products in clinical development. Given the long historic commitment of the industry to the blockbuster model of drugs for mass markets, this represents a fundamental change in the material and technological components of the pharmaceutical regime and the formal and informal rules that govern it (see Table 2). At first sight, it seems hard to understand. The next section will analyse a series of economic drivers and regulatory changes that have made this switch possible and driven the growth of targeted therapies.

Capitalizing on targeted drugs and segmented markets

As highlighted in the conceptual framework, the contemporary pharmaceutical industry is highly financialized and driven by a model of intellectual monopoly capitalism that enables the extraction of rents from large patent portfolios. In this context, companies seek to maximise their return on investment and create monopolies that enable high prices with reduced competition where IP protection can be extended. The shift to targeted therapies has achieved these objectives in a new way. The following section will demonstrate how targeted therapies experience easier regulatory pathways, are cheaper to develop, have higher success rates, ensure greater monopoly, and have higher prices.

Faster and easier regulation of targeted therapies

To speed up the approval of medicines, both the FDA and EMA have introduced a series of expedited regulatory pathways. The first of these was established by the FDA in 1988 with 'Fast Track', followed by 'Accelerated Approval' and 'Priority Review' - both in 1992, and finally, 'Breakthrough Therapy Designation' was enacted in 2012. Similar measures were introduced by the EMA (Accelerated Assessment and PRIME) a few years later. These programmes facilitated targeted drug development in three ways:

Fostering engagement with regulatory agencies: several pathways aim to enhance early and frequent communication between drug sponsors and regulators to support more efficient development.

Shortening the review timeframe: a number of pathways enable earlier market access under certain conditions, often requiring post-approval commitments.

Lowering the threshold of clinical evidence requirements: a number of pathways allow regulatory flexibility in the level of clinical data required at the time of submission. FDA Accelerated Approval is for serious conditions that fill an unmet medical need, where the drug can be approved based on a surrogate or intermediate clinical endpoint to make market access easier.

Whilst the use of these pathways has reduced approval times and allowed a greater number of medicines to reach the market, they have been extensively criticised for lowering evidential standards in drug assessment both in terms of a greater risk to patient safety and for allowing drugs onto the market with little or no evidence of efficacy (Davis, Lexchin et al. 2016).

An analysis of orphan approvals granted by the FDA shows that a significant proportion benefit from expedited regulatory pathways. Between 2011-20, 37% received Priority Review, while 17% were granted Fast Track designation and 16% received Breakthrough Therapy Designation. Additionally, 10% of orphan drugs were approved through the Accelerated Approval pathway. Overall, nearly half (49.7%) of FDA orphan drug approvals were granted at least one expedited review designation, and among these,

half involved two or more expedited programmes. Of the 119 Breakthrough Therapy Designations granted between 2017-22 72% were for orphan drugs (Kashoki 2023). One consequence of earlier approval on the basis of more limited evidence is that a significant number of orphan drugs approved in this fashion later showed patient safety problems and/ or a lack of efficacy (Michaeli, Michaeli et al. 2024).

Targeted cancer therapies also make extensive use of expedited pathways, particularly Accelerated Approval (Tibau, Hwang et al. 2024) and Breakthrough Therapy Designation, with over half of all BTD applying to cancer drugs (Collins, Stewart et al. 2022). A detailed cohort study of 50 molecular-targeted anti-cancer drugs (covering 84 indications) approved by the FDA between 2015-22 (Tibau, Hwang et al. 2024) found that 87% were granted Priority Review, 60% received Breakthrough Therapy Designation, and 69% also received orphan drug designation. In addition, 38% were granted Accelerated Approval. There was a clear pattern of approval on the basis of more limited evidence than for standard drug assessment. The study also concluded that fewer than one-third of these demonstrated substantial patient benefits at approval.

The extensive use of expedited review pathways made by targeted therapies, particularly in the US, has been important in reducing the time and cost of drug development, and enabling greater numbers of these products to be approved on the basis of more limited evidence. This provides an important incentive for industry to invest in these products. It also marks an important change in the governance of the pharmaceutical regime as conceptualised by the MLP (see Table 2), with new evidential standards and epistemologies (e.g. move to post-marketing evaluation) that enables targeted products to reach the market more quickly and easily.

Targeted therapies are cheaper to develop and have higher success rates

It is hard to accurately establish many of the costs involved in pharmaceutical research and development given a general lack of financial transparency in the industry. The cost of developing a new medicine is

contentious and estimates vary considerably depending on the methodology used (see Hanchard, 2025). Despite this, a number of studies have attempted to quantify the costs of developing both orphan drugs and targeted cancer therapies compared to non-targeted medicines.

The clinical development of drugs for rare diseases has several advantages that make them cheaper to get from bench to bedside. These include the very limited size of patient populations which make small trials the norm (and large trials impossible). Set against this are difficulties in patient recruitment as it can be hard to get enough participants for a traditional clinical trial and this means that clinical development times are no quicker than for non-orphan products (Michaeli, Jürges et al. 2023) This challenge has stimulated the development of novel trial methodologies which allow smaller numbers and regulatory approval at an earlier stage on the basis of more limited evidence. Orphan designation also provides tax credits on the cost of clinical trials and waivers for the fees involved in regulatory submission. A major study of the cost of development evidenced the outlay (capitalized clinical cost) for a manufacturer to bring an approved orphan drug to market at $291M, compared to an outlay of $412M for non-orphan products Jayasundara et al. (2019). In terms of success rates in clinical trials, a number of studies have shown that orphan drugs have significantly higher success rates than non-orphan products (Michaeli, Jürges et al. 2023)

Targeted cancer therapies are also cheaper to develop as they are designed for patients with specific genetic mutations or biomarkers, which delineate the trial population and allows for more efficient study designs. They are generally based on a better understanding of disease biology, where drugs are matched to specific molecular targets, allowing faster trial enrolment, shorter development times and higher success rates. A study by the trade body BIO demonstrated that targeted cancer therapies have a higher clinical development success rate compared to non-targeted therapies (BIO 2016). In terms of the cost of development (Henderson et al. (2023) calculated that bringing a precision oncology medicine to market cost $1.1Bn less ($3.5Bn) than for a non-precision oncology medicine between 1997 and 2020. Although the cost of manufacturing targeted cancer drugs may be greater than non-targeted therapies,

the evidence on this is limited and the WHO found that the cost of production is only a small component of total costs and does not account for the high price of these medicines (WHO 2018). Whilst the reduction in cost and increased success rates of developing targeted therapies is important, this is not a fundamental change in the pharmaceutical regime itself, but provides another incentive to invest in these products.

Sustained monopolies for targeted therapies

The introduction of orphan legislation was designed to extend industry's monopoly rights to address market failure regarding drugs for rare diseases. As illustrated above, this has been very successful with consistent growth in orphan approvals, particularly in the US. One feature of this growth has been an increase in the number of approvals for each drug molecule, so that among the leading companies with more than ten FDA orphan drug approvals between 1983 and 2022, these products have, on average, received approval for more than two distinct orphan indications (analysis of Pharmaprojects data). In several cases, individual drugs have been approved for over ten orphan indications. The increasing use of multiple orphan indications is one of the ways in which companies are seeking to further extend monopoly rights both in terms of disease areas but also over time, as additional indications extend the period of exclusivity on that product for a given indication by seven years. In principle, generic or biosimilar competition could enter the market for the indications that are now without regulatory exclusivity even if other (orphan) indications are still covered. However, in many cases this does not happen in practice as the barriers to market entry remain significant and the commercial incentives insufficient.

Orphan drugs are also exempt from the Medicare price negotiations on high drug prices contained in the 2022 Inflation Reduction Act (IRA) which aimed to reduce the Federal prescription bill. Previously Federal agencies were not allowed to negotiate bulk price discounts. It is estimated that this exception has cost the US taxpayer between $1.1Bn- $3 Bn a year (Vogel, Zhao et al. 2024).

Given that roughly half of all orphan drugs are for the treatment of cancer there are a large number of targeted oncology therapies that also have at least one orphan designation. It is possible for a targeted therapy to have multiple orphan indications as well as being licensed for more common cancers. Four of the top 10 selling drugs in the world in 2024 had this pattern of multiple indications and orphan approvals giving them significantly greater market exclusivity.

Targeted cancer therapies enjoy greater patent protection than similar non-targeted therapies in other ways. There is often a high level of patent activity around these products as a means of creating patent thickets (overlapping patents on formulations, administration methods, and biomarkers) to extend exclusivity. Patenting related to biomarkers used to target cancer therapies is another area of growth, giving additional market exclusivity. Biomarker patenting is complex as they cannot be granted on natural correlations (e.g. biomarker A predicting disease B) without a “transformative step”. But they are granted if a particular biomarker is linked to a drug response in a specific cancer sub-type or are the basis of innovative detection methods or platform technologies. The European Patent Office (EPO) reported a major rise in cancer-related patenting with a steep increase in the last decade. In 2021 alone over 13,000 cancer-related International Patent Families (IPFs) were filed, with many on targeted cancer therapies and related biomarkers (EPO 2024). Many targeted cancer therapies are also hard to develop and manufacture (e.g. immunotherapies). It is a major barrier to the entry of both generic and branded competition. This has been recognised as an important barrier to lower drug prices and is part of the motivation behind the establishment of the FDA’s Drug Competition Action Plan.

The rapid growth of targeted therapies rests on the expansion of regulatory exclusivity first enabled by the ODA. This fundamentally changed the incentive structure within the sector and has in part motivated the stratification of common diseases such as cancer. In this sense, there has been a transition in the economics of the pharmaceutical innovation system that has fundamentally altered the financial opportunities open to innovators.

Higher prices

A major consequence of the lack of competition and the increasing monopoly enabled by the rise of targeted therapies has been a dramatic increase in the price of drugs in some therapeutic areas. Over the last two decades, the cost (to payers) for new medicines has rapidly increased, especially for oncology (see Michaeli, Jürges, and Michaeli, 2023) and rare disease – therapeutic areas whose treatments comprise 54% of manufacturers' total revenue (IQVIA, 2024a, p. 48). The 2023 median cost to payers across all 22 non-oncological orphan medicines launched in the USA was $273,000, with an annual median of $299,000 for their orphan oncological counterparts (Ibid.). Meanwhile, the median annual cost for specialty medicines outside oncology and rare diseases were just $44,000 in 2023 – albeit still over eight times that of traditional (non-speciality) drugs (IQVIA, 2024a, p. 49). Previously, the median US launch price for an orphan drug between 2017-2021 sat at $218,872 while their non-orphan counterparts launched at a median of $12,798 (Althobaiti et al., 2023) - showing a sizable and growing disparity. Beyond the US, Dane et al. (2023) also evidence a CAGR of ~16% for orphan drug costs between 2000 and 2020 across major European countries like Denmark, France, Germany, and the Netherlands. Not only have prices increased faster for orphan than non-orphan drugs for most of the world, within rare oncology drugs at least, prices have risen by over 50% in recent years (Michaeli, 2023).

These increasing prices are rationalised and justified within health policy and ethical debates about the rule of rescue as a moral imperative to save identifiable lives in immediate danger at any expense (Largent and Pearson, 2012, p. 27). At the same time, notions of outcomes-based or value-based treatment pricing have been proposed as counter measures to temper price rises. However, whilst these ideas have been in circulation for several decades their overall uptake has been modest at best (Garrison Jr. et al., 2023, p. 73).

Understandably, questions have arisen over the cause of such high (premium) prices for orphan drugs and targeted cancer therapies. As a hotly contested topic within both normative and empirical health

economics (Hanchard, 2025), it is here that some scholars accuse pharmaceutical and biotechnology companies of misusing policy incentives intentionally to excessively profiteer, engaging in monopoly capitalism to do so (Bourgeron and Geiger 2022) – despite targeted therapies costing less to develop. Industry is charged with effectively rigging the market to artificially heighten prices and doing so at the cost of putting strain on healthcare systems worldwide. Other scholars counter that the reported costs for orphan drugs and targeted cancer therapies to payers are often based only on publicly available list prices, whilst the actual negotiated (secret and commercially sensitive) net prices charged to payers are often much lower (Cassier, 2021; Russo et al., 2021). Meanwhile, others stress the longer-term commitment and need for higher (differential) prices in high-GDP countries such as the US to offset lower costs in low- and middle-income countries (LMICs) for global equity of access (Lichtenberg, 2010). Although the justification for such high prices is contentious, as we have shown above, the cost of targeted therapies is undeniably high and rising quickly. The shift to these very high prices marks an important transition in both the threshold that purchasers are willing to pay for a therapy and the business models within the industry. It represents an important change in the normative “rules”, as understood within the MLP (see Table 2), that have historically governed the pricing of medicines and the commercial opportunities this affords.

Discussion: A changing regime?

This paper has demonstrated that there is an important transition underway within the pharmaceutical sector towards a new regime we have labelled “premium pharma”. The key sociotechnical features of this shift and the emerging regime are summarised below in Table 2. This is largely heuristic and uses the framework provided by Geels’ Multi Level Perspective. It must be stressed that the move to such a new regime is uneven, partial and incomplete and may only ultimately affect a portion of the pharmaceutical industry.

Table 2: Summary of main features of standard and premium pharma regimes

Firstly, the material and technological components of the regime. The market based definition used here highlights important shifts in the focus of pharmaceutical product development and a move away from mass blockbusters towards niche and segmented markets. This has been enabled by technological developments in genomics, and the growing identification of molecular biomarkers and novel therapeutic modalities which has made possible the stratification of common diseases including many cancers. The emergence of premium pharma has been, in part, a response to long-standing problems in developing blockbuster products.

Secondly, the formal and informal "rules" that guide biomedical practice and commercial decision making. In particular, the changing understanding of disease nosology as more conditions were seen as rare or small sub-sets of common diseases. This shift coincided with the rise of rare diseases as an important category in clinical medicine, politics and policy. The demonstration that drugs for niche and segmented markets could be highly profitable was important in the emergence of new business models which were first adopted by dedicated biotechnology SMEs and later incorporated into the mainstream industry.

Thirdly, the changing regulatory landscape was a key factor supporting the success of these approaches, most notably the Orphan Drug Act and subsequent introduction of a series of expedited drug assessment pathways. Although not restricted to targeted therapies, they have made extensive use of these provisions which enable easier market access on the basis of more limited evidence. Such policies have also played an important role in reducing the cost of clinical development for targeted therapies and improving their success rates.

Fourthly, normative rules around monopolies and expectations about the price of medicines. As discussed earlier, the main determinant of pharmaceutical companies' behaviour within a highly financialized economic sector is the creation of intellectual property monopolies on the exploitation of intangible assets and the search for market exclusivity. This has been achieved via both the patent

system and government agencies granting regulatory exclusivity. The development of targeted therapies has been powerfully influenced by intellectual property law in a number of ways, including the patenting of molecular biomarkers and the creation of patent thickets. The best example of regulatory exclusivity is the Orphan Drug Act itself, which has proved highly successful in creating new monopolies and changing industry behaviour. The analysis presented here also demonstrates multiple other ways in which regulatory provisions have further entrenched the monopoly position of companies in relation to targeted therapies, in particular allowing multiple orphan indications on a single drug molecule and the exemption of orphan drugs from US Federal price controls.

The net result is the ability of industry to charge very high and rapidly rising prices for these targeted products, which is becoming increasingly normalised. This is a good example of the political economy of intellectual monopoly capitalism as set out by Rikap (2021). An important contribution of this paper is to highlight how regulatory exclusivity granted by the ODA has played a central role in the process of assetization associated with targeted therapies. This is most visible in the case of drugs for rare cancers now constituting the single biggest category of new medicines in development.

The use of the Multi Level Perspective demonstrates how the emergence of premium pharma has depended on parallel sociotechnical changes in the underlying technologies of drug innovation, the political economics of clinical development, changing disease concepts and new industry business models and investment strategies, the regulation and governance of drug approval, and the sanctioning of greater monopoly control and high drug prices. It can therefore be seen as a process of co-construction

between these different domains with changes in one opening up and shaping new possibilities in other areas. Taken together they constitute a sociotechnical transition in this part of the pharmaceutical sector. The framework established here also provides a means for empirically operationalizing and testing the extent to which other pharmaceutical technologies are moving towards a premium pharma model. Metrics to assess this are proposed in Table 2.

These changes have been pioneered in the United States and greatly enabled by the active role of the US Federal government. The US is increasingly the centre of the global pharmaceutical industry as the site of most drug R&D, new product launches and profit. Government regulation has been critically important, firstly in the passage of the ODA, but later in the regulatory reforms that led to the creation of expedited drug approval pathways, as well as the limited evaluation of the cost effectiveness of medicines, legal measures shaping the IP environment, and restrictions on the ability of Federal agencies to control drug prices.

A detailed analysis of the diffusion of the premium pharma regime internationally is beyond the scope of this study, but it is worth reflecting on changes occurring in Europe to highlight some important differences that may limit the entrenchment of premium pharma in other territories outside the US. The growth of targeted therapies in Europe exhibits some of the core elements of the premium pharma regime as summarised in Table 2. These include the increase in orphan drug approvals, adoption of nichebuster business models by some large European pharmaceutical companies (e.g. AstraZeneca), and changes in disease nosology which are transnational. However, other elements of the premium pharma regime are either less apparent (e.g. EU use of expedited review processes – see regulation section) or have been resisted (e.g. very high drug prices). The latter is well illustrated by the refusal of several European countries to pay for expensive medicines approved in the US, on grounds of lack of cost effectiveness ((Stawowczyk, Malinowski et al. 2019). This reflects a key difference between Europe and the US healthcare systems in the governance of drug expenditure, most notably the much wider use of health technology assessment in Europe.

Conclusion

This paper breaks new ground in examining the changing political economy of the pharmaceutical sector and the emergence of a new sociotechnical regime around premium pharma. There are a number of important implications. The first of these is the continued fragmentation of disease categories and drug markets which is inherent in the changes we have described. It seems highly likely that the number of rare diseases and the sub-setting of common conditions will continue to grow, fundamentally changing how diseases are understood and treated.

Secondly, there are important challenges posed by the rise of premium pharma for public payers in many countries outside the US (e.g. Europe, Canada, Australia, Japan). In particular, the high and rapidly increasing prices for some of the most innovative medicines places an increased burden on welfare based healthcare systems. This has already led to a number of drugs only being reimbursed at a significantly lower price in Europe compared to the US and there is evidence that a high proportion of new US approved orphan drugs are not being launched in Europe for commercial reasons related to price and reimbursement differences (author paper under review). This has become a contentious geopolitical issue between the US and European states, with the UK having to agree much higher drug prices following tariff negotiations with President Trump and a threatened investment boycott by a number of large pharmaceutical companies.

Most importantly, the third main implication is the impact that the move to premium pharma is likely to have on global access to advanced therapies. The very high prices charged for many targeted products means that these will only be available in a handful of Global North high income countries, most notably the US, and are very unlikely in the short term at least to be accessible in most LMICs in the Global South without extensive differential pricing controls. This is not some oversight on the part of the pharmaceutical industry, but is inherent in the business strategies underpinning the shift to premium pharma which aim to charge excessively high drug prices and maximise return on investment. In this sense, unequal access

is inherent in the design of this new regime and industry calls for access for all to these new therapies are little more than performative. There are ways in which the targeted therapies described in this paper can be made available globally in the longer term, but this will require the development of alternative innovation models e.g. SPINs (Douglas, Aith et al. 2022) that explicitly aim to address global inequalities in access and will require the active support of government, professionals and patients.

CRediT authorship contribution statement

Paul Martin: Writing – original draft, Funding acquisition, Data curation, Conceptualization. Jin Ding: Writing – original draft, Methodology, Data curation. Matthew Hanchard: Writing – original draft, Data curation.

Ethics statement

Prior ethical approval was obtained from the University of Sheffield institutional ethics committee prior to data collection.

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Data availability

Most of the data is publicly available apart from that gathered from the Phrmaprojects database. The collated data will be deposited in an open access data repository.

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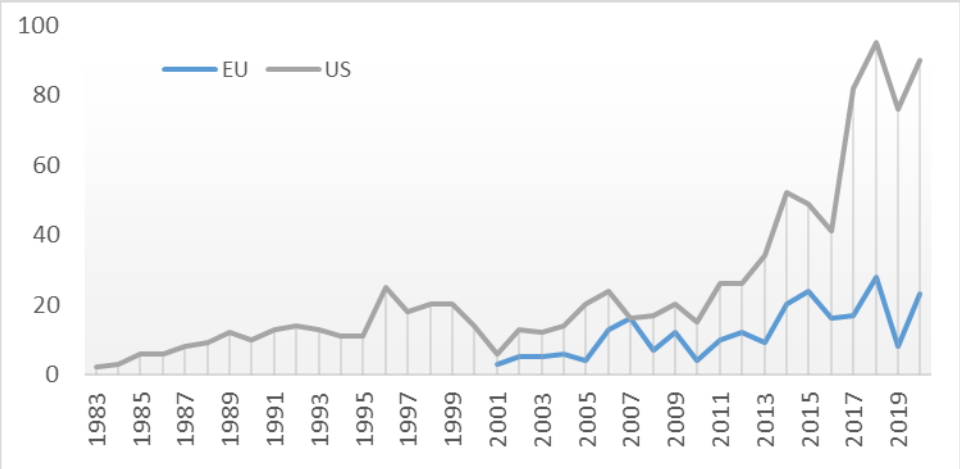
Graph 1: Growth in annual orphan approvals by FDA and EMA (1983-2020)



Note: EMA only introduced orphan legislation in 2000

Table 2: Summary of main characteristics distinguishing traditional and premium pharma, regimes, and metrics to distinguish between them

Domain	Traditional	Premium	Metric
Product (material and technological component)	Standard therapy based on undifferentiated patient population	Targeted therapy aimed at rare diseases or sub-sets of common diseases (e.g. cancer)	Extent to which products are aimed at small niche markets
Business model and market (formal and informal rules)	Blockbuster products aimed at undifferentiated mass markets	Nichebuster products aimed at sub-sets of patient populations	Adoption of nichebuster business models that sell premium prices products
Disease nosology (formal and informal rules)	Highly prevalent common diseases (whole population)	Rare diseases and newly created sub-sets of common disease defined by molecular biomarkers	Disease targets defined as rare
Governance (regulatory frameworks)	Standard review process based on extensive evidence collected in large (Phase III) clinical trials	Move to earlier approval in expedited pathways on basis of more limited, small scale (Phase II) evidence with post-marketing follow-up	Extent of use of expedited pathways
Pricing (normative rules)	Moderately priced but with shift to higher priced secondary care products	High/ very high and rapidly increasing premium prices	Ability to charge very high and rapidly increasing premium prices