Analysis

High drug prices are not justified by industry's spending on research and development spending

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KEY MESSAGES

- From 1999 to 2018, the world's 15 largest biopharmaceutical companies spent more on selling, general, and administrative activities ($2.2 trillion) than on research and development ($1.4 trillion), although the gap narrowed over time.
- Most of these companies also spent more on share buybacks and dividends than on research and development.
- Most new medicines developed during this period offered little or no added benefit over existing treatments, making it difficult to sustain the argument that high prices are needed for valuable innovation.
- The biopharmaceutical industry could generate more medically valuable innovation with existing resources using affordable pricing, but government action would be needed along the lifecycle of new medicines.

Contributors and sources

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Patient involvement

No patients were involved.

Conflicts of Interest

We have read and understood BMJ policy on declaration of interests and have the following interests to declare:

AA declares past research grants from Novartis and Krystal Biotech, advisory fees from the European Commission, and shares ownership in a health tech company developing software tools for decision-making; none relate to the topic of this work. RP was previously employed in the mergers and acquisitions team of Roche's diagnostics division.

High drug prices are not justified by industry's spending on research and development

Angelis and colleagues question the industry's claim that high drug prices are necessary to sustain valuable medical innovation. They examine the amount spent by biopharmaceutical companies on research and development vs other budget items, like marketing and share buybacks, and they also review the evidence around the added clinical benefits of new drugs.

The longstanding debate over fair drug pricing

Concerns over the prices of new medicines have been growing over the past decade. In the US, estimated net prices of newly launched prescription drugs have increased from a median of around $1,400 in 2008 to over $150,000 in 2021.[1] Zolgensma, a gene therapy approved by the US Food and Drug Administration (FDA) in 2019 for spinaly muscular atrophy, was at the time of approval the most expensive drug ever, with a price of over $2 million for a single dose treatment.[2] Several more recent rare disease drugs are priced even higher,[3] with Hemgenix becoming approved by the FDA for hemophilia B in November 2022, becoming the newest most expensive therapy at $3.5 million per dose.[4] But even old and very common medications have seen inexplicable price increases: in the US, the list price of some insulin products has increased more than 2-fold from 2007 to 2018[5], while a US government report identified 1,216 products whose prices rose above inflation between July 2021 and July 2022, with an average increase of 31.6% but in some cases much more. For example, the price of sulfasalazine, first approved in 1950, increased by 100% over this period, while the price of fluconazole, available since 1988, increased by 1000%.[6]

The biopharmaceutical industry has long argued that high prices are needed to sustain research and development (R&D) for new medicines. When asked to justify a price tag of $10,000 per month for a drug used to treat prostate cancer, a senior executive at Johnson & Johnson responded: "The easy diseases have largely been solved. It gets harder and harder as we go after new treatments for ever more challenging diseases."[7] Pharmaceutical companies frequently note how their shareholders and investors could easily shift their investments to other more profitable and less risky sectors. Indeed, there are large financial risks associated with bringing new medicines to market, as many candidate molecules will not make it because they are ineffective or harmful, or both.

There are, however, reasons to be sceptical of these arguments, given that the pharmaceutical industry is one of the most profitable sectors.[8,9] Although comparisons of

profits by the pharmaceutical and other industries are complicated due to accounting rules,[10] data suggest that pharmaceutical companies are particularly profitable, even after adjusting for R&D spending as a share of revenues.[8] There also seems to be a disconnect between product R&D costs and prices. One recent study found no association between how much pharmaceutical companies spend on R&D and the prices they charge for new medicines.[11] The industry's justification of high drug prices also ignores the sizeable public investments into drug discovery and development, which has contributed to the basic and translational research underpinning all new drugs approved by the US Food and Drug Administration (FDA) from 2010 to 2016;[12] more than 1 in 4 new drugs approved by the US FDA from 2008 to 2017 were linked to public investment during the late stages of development.[13] This means that society is potentially paying twice for new drugs, first in the form of publicly-subsidised research and second through high product prices.[14]

As we show in this Analysis article, the largest biopharmaceutical companies spent more over the past two decades on selling, general and administrative (SG&A) activities—a heading that includes almost all business costs not directly attributable to making a product or performing a service, including marketing and advertising—than on R&D, which includes both preclinical and clinical research. In most years, these companies also spent more on share buybacks. Taken together with evidence that most new medicines offer little added benefit over existing therapies, this makes us question the claim that high drug prices are needed to sustain R&D for valuable innovation.

Biopharmaceutical companies spend more on SG&A and share buybacks than on R&D

Based on publicly available financial reports from 1999 to 2018, the 15 largest biopharmaceutical companies earned a total of $7.7 trillion in revenues from 1999 to 2018. Over this period, they spent $2.2 trillion on SG&A activities and $1.4 trillion on R&D (Figure 1). The precise details of what is included within R&D and SG&A activities can be unclear, with boundaries somewhat blurred. For example, companies may conduct so-called seeding trials as part of the reported R&D spending, with these trials having been described as “company-sponsored trials of approved drugs that appear to serve little or no scientific purpose”,[15] and considered by some as marketing strategies.[16] Notwithstanding this limitation, it is clear that companies spent more on SG&A than on R&D every year from 1999 to 2018, which is consistent with earlier evidence from 1975-2007.[17]

Most of the same companies also spent more buying their own stocks, a practice known as share buybacks, than on R&D during this period. Share buybacks are expected to lift share prices and thus benefit shareholders, including senior company executives whose income is often directly linked to the share price. A drug pricing investigation by the US House Committee on Oversight and Reform revealed that, from 2016 to 2020, the 14 largest pharmaceutical companies spent $577 billion on share buybacks and dividends—$56 billion more than on R&D—at a time when annual executive compensation grew by 14%.[18] The findings of the Committee's report were consistent with earlier findings by the Institute for New Economic Thinking.[19] Using data from 2006-2015, the Institute found that 18 large US pharmaceutical companies spent more on share buybacks and dividends than on R&D,[19] seemingly prioritising short-term financial returns over long-term investments in innovation. This spending reflects the growing financialisaton of the pharmaceutical industry in the past decades, which has generally focused on maximising shareholder value.[20] At the same time, share buybacks may signal that a company has more cash than investment opportunities (that is, there are not enough potentially profitable projects to enter into the portfolio), and therefore the company chooses to return "unproductive" cash on the books to shareholders. However, if excessive buybacks take place repeatedly over many years, it raises questions about commitments to truly valuable and risky biopharmaceutical R&D.

While companies spent more on both SG&A activities and share buybacks than on R&D over the past two decades, SG&A expenses (as a share of revenue) dropped from 35% to 27% over this period while R&D spending increased from 16% to 21% (Figure 2). This is consistent with data for the 10 pharmaceutical companies with the largest R&D budgets between 2005 and 2015.[21]

We also know that pharmaceutical companies engage in mergers and acquisitions to access promising new products.[22] Alongside evidence that large pharmaceutical companies are not involved in the discovery of most new drugs,[23] this suggests a shift of strategy from early-stage research and discovery to late-stage acquisition and development.

The real innovation crisis: most new drugs provide no added clinical benefit

While manufacturers, regulators, payers, clinicians, and patients may differ in their views of what constitutes pharmaceutical innovation, Light and Lexchin argued that the "real innovation crisis" in pharmaceutical R&D does not relate to the absolute number of new drugs approved, but rather the proportion representing therapeutic advances.

In the 1970s and the 1980s, it was estimated that around 1 in 6 (16%) new drugs approved by the US FDA offered important therapeutic gains, based on FDA-assigned scores.[24] Another study covering products approved from the mid-1970s to mid-1980s found that only 1 in 10 (11%) new drugs globally were therapeutically and pharmacologically innovative.[25] These figures are consistent with several other recent studies, suggesting that only a small fraction of new drugs offer major clinical benefits (Table 1).[26-31] Analyses of drug evaluation reports put out by health technology assessment bodies in France and Germany in the 2010s suggest that the majority of new drugs offer no added clinical improvement, with only a fraction offering important or major improvements.[32-36] Another recent study from the Belgian Health Care Knowledge Centre concluded that there was considerable uncertainty about the benefits of many new cancer drugs measured by overall survival and quality of life, despite an increase in their prices.[37]

On the positive side, the majority of products under development during 1997-2016 targeted novel mechanisms of action.[38] At the same time, though, we have seen a shift in R&D focus from “blockbuster” drugs, typically targeting chronic diseases and sold in high volumes globally, to “nichebuster” drugs targeting rare diseases or narrow indications for which high prices can be charged. Publicly available FDA data show that the proportion of drug developed for rare diseases has increased over time from 25% of all approvals in 2001-2005 to 48% in 2016-2020.[39] In 2021, orphan drugs accounted for 52% of all approvals.[39] This is probably due, in part, to companies targeting additional market exclusivities and other incentives granted for rare disease drugs,[40] alongside regulators’ willingness to relax evidentiary requirements in case of unmet health need and payers’ higher willingness to pay for these products.

Not only have past spending patterns not delivered a pipeline of truly innovative drugs in terms of added therapeutic value, but many health needs remain unmet by the current pharmaceutical business model. This includes neglected diseases, antimicrobial resistance, and other emerging infectious diseases.[41] Most biopharmaceutical R&D investments are aimed at maximising shareholder value, leading companies to pursue drug products that can be sold in commercially attractive markets, with extensive marketing to support this goal. This is, in part, why companies invest heavily advertising directly to consumers, sponsoring scientific meetings, and distributing free samples to doctors and patients.[42] In many important markets, the current system rewards new products irrespective of comparative advantages or contribution to public health priorities,[43] which in part reflects the fact that

regulatory authorities are tasked with evaluating new drugs based on their individual benefit-risk balance rather than the demonstration of added clinical benefits.[44]

Another root cause of the misalignment between the R&D outputs and people's health needs is that the main economic incentive for medical innovation is the award of patents, which in turn provide companies with monopoly powers that keep competition at bay and allow to charge high prices and boost profitability. And patents are awarded based on chemical novelty and inventiveness of the product, independent of the therapeutic benefit a product may, or may not provide. As a consequence, companies prioritize R&D on patentable products that can be sold in the market, rather than medical breakthroughs or addressing people's health needs *per se*.

Biopharmaceutical innovation must serve public health objectives

Over the past two decades, pharmaceutical companies have spent more on SG&A activities and share buybacks than on R&D, at a time when the costs of many of its components have fallen. Many of the roles once undertaken by humans, such as switchboard operators and typists, have disappeared. Costs of travel have fallen as the quality of teleconferencing has increased. Similarly, the growth of the internet has permitted advertising to have a much greater reach than was possible with promotional material in journals or delivered by sales representatives. Yet even though R&D spending increased, most new drugs developed still provide little or no added therapeutic value. It thus seems hard to justify the claim that ever-rising high drug prices are necessary for companies to continue investing in R&D for valuable innovation, to come up with new and better drugs.

In theory, the biopharmaceutical industry could generate more medically valuable innovation with its existing resources, without passing R&D costs on to patients and health care systems in the form of ever higher and increasingly unaffordable prices. For this to happen, government intervention or regulation would be needed along the lifecycle of new medicines. Possible government actions include reforming national patent systems to make patent awards more stringent, to avoid rewarding chemical novelty and inventiveness independent of therapeutic value; clear communication by public health authorities to lay out health needs-focused R&D priorities and the strategic use of public research funding to support those; smarter allocation of public research funds with retention of (partial) ownership that can be leveraged to pursue public health objectives, including affordable pricing; raising evidence standards for market authorisation by requiring companies to conduct comparative

clinical trials designed to establish added therapeutic value whenever possible; reforming pricing and reimbursement systems to reward companies that develop drugs that deliver added clinical benefit and disincentivize me-too and evergreening strategies (Table 2). With the exception of comparative clinical benefit assessment approaches for pricing and reimbursement adopted by several health technology assessment bodies, the other interventions (which would occur during earlier stages of medicines' lifecycle) have largely remained unimplemented, although this could change if the political will were there.

For specific therapeutic areas where market incentives seem inadequate, such as antibiotics for patients with drug-resistant infections, a comprehensive set of "push" and "pull" incentives for manufacturers may be needed. The former include research subsidies to lower R&D costs, while the latter include outcome-based rewards to guarantee financial returns (e.g., advanced market commitments).[45] Although such mechanisms have been implemented in several contexts, ranging from R&D subsidies for diseases with unmet need, to advanced market commitments for vaccines, they could be more strategically re-oriented to promote both socially desirable innovation and affordable prices. For example, the UK, in 2022, implemented a subscription-style payment model (i.e., "pull" incentive) for two new antimicrobial drugs.[46]

Increased transparency around medicine pricing, patent status, R&D costs, and clinical trial data, as recommended in a 2019 World Health Assembly resolution, could help redefine the social contract between all stakeholders involved in drug development and align incentives towards public health goals. As the WHO Council on the Economics of Health for All has argued,[47] the economic, fiscal, and industrial policies governing the sector must be redesigned to improve health outcomes and ensure that health innovation is for the common good.

When designing and implementing government interventions, including drug pricing policies, it is important to examine the impact of such measures on both inputs (e.g., R&D investments) and outputs (e.g., health outcomes) over the long term, in order to determine the full implications of the intervention and make well-informed decisions. This also requires detailed financial analyses, ideally considering more accurate metrics than mere profit margins, such as return on equity, to better understand the impact on investors decisions and the potential knock-on effects. The non-partisan US federal Congressional Budget Office has estimated that the prescription drug provisions in the Inflation Reduction Act (which, among other things, allows Medicare to negotiate the prices of some medicines) will save billions per year and likely only lead to a modest decrease in the number of new drugs

developed over the next 30 years (decrease of 1%).[48] This might be an acceptable trade-off, especially if many of the drugs we would go without would be low-value ones.

Past spending patterns by biopharmaceutical companies, alongside evidence on the clinical benefits of new drugs, suggest that high drug prices are not justified on the grounds of sustaining R&D for valuable innovation. Biopharmaceutical companies seem to charge as much as each market can bear, with pricing focused on maximising revenues. A transition is needed towards fostering the development of therapeutically superior drugs that can enhance patient outcomes. This may require a shift of more resources from SG&A to R&D activities and companies to prioritise disease areas with clinical unmet needs. Governments, policy makers, drug regulators, health technology assessment bodies, and payers need to re-think the incentives for valuable biopharmaceutical innovation, creating policy and regulatory environments that will meet public health objectives. These stakeholders should ensure that the current supply-driven R&D portfolios can improve the world's population health by addressing unmet medical needs, improving our therapeutic arsenal, and ensuring equitable access. The world needs a truly value-based health care system for incentivising and rewarding improvements in health outcomes and population health.

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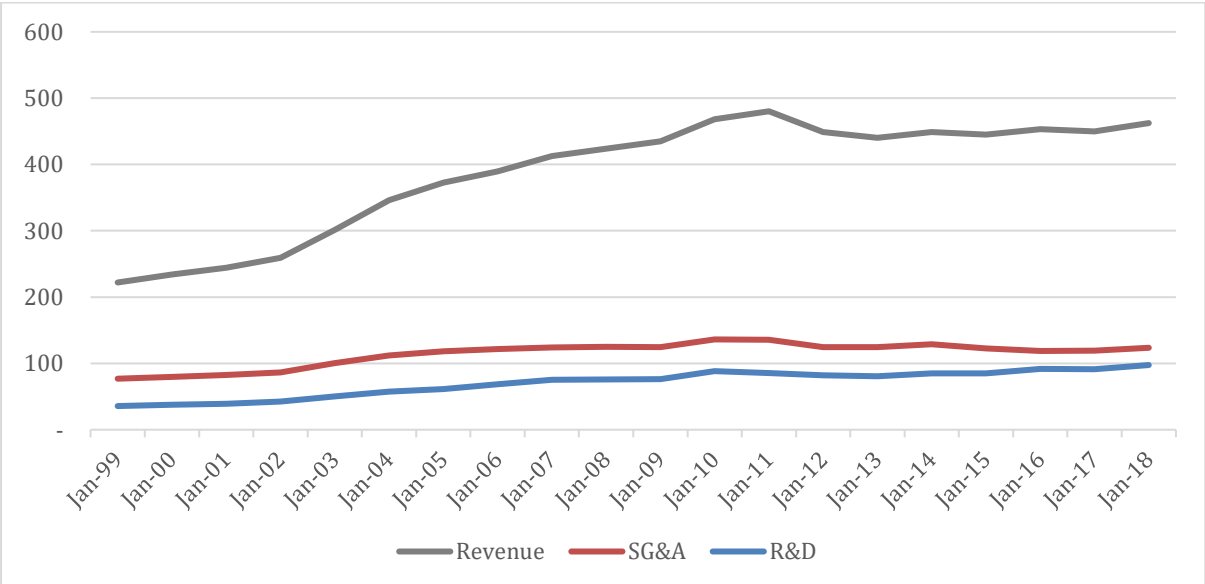
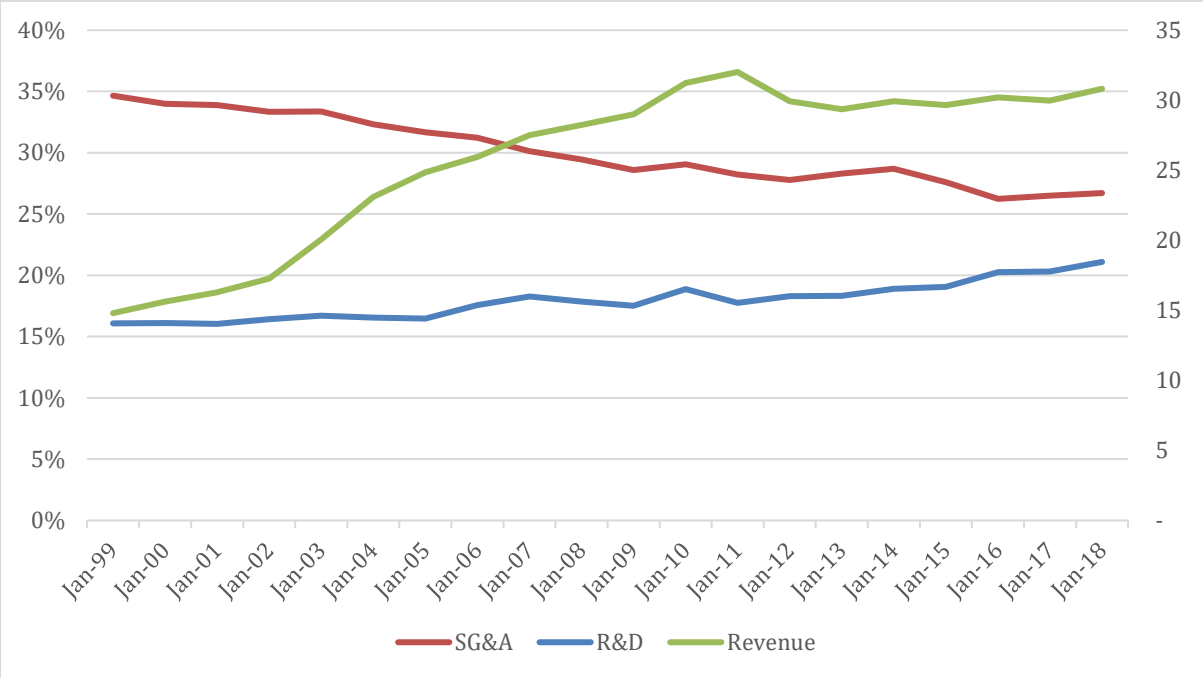
Figure 1: Total revenues, SG&A spending and R&D spending (US$ bn) for the 15 largest biopharmaceutical companies, 1999-2018



Note: R&D indicates research and development; SG&A, selling, general, and administrative (activities). Sources: Data were obtained from US company annual and quarterly forms filed with the United States Securities and Exchange Commission and non-US company annual financial reports.

Figure 2: Average SG&A expenses vs R&D spending (% of revenue, left Y-axis) and revenue ($ billion, right Y-axis), for the largest 15 pharmaceutical companies in 1999-2018



Note: R&D, research and development; SG&A, selling, general, and administrative (activities).

Sources: Data were obtained from company annual and quarterly forms filed with the United States Securities and Exchange Commission and company annual financial reports.

505 **Table 1:** Review of studies assessing the added therapeutic benefits of new drugs

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Study	Time period	Country	Drug sample	Rating / assessment	Clinical benefit
Kaitin et al, 1991[24]	1978-1989	US	218 new FDA approved drugs	FDA ratings	16% offered important therapeutic gains
Barral, 1996[25]	1974-1994	International	new marketed drugs	Authors	11% therapeutically and pharmacologically innovative
Morgan et al, 2005[26]	1996-2003	Canada	1147 CPMPRB appraisals	Authors based on the CPMPRB classifications	68 (6%) "new breakthrough" 74 (7%) "me-too breakthrough" 1005 (88%) "without substantial improvement over existing products"
Motola et al, 2006[27]	1995-2004	EU	176 EMA approvals	Authors based on Motola's rating system	49 (28%) with an important degree of therapeutic innovation
Luijn et al, 2010[28]	1999-2005	EU	122 EMA approvals	Authors based on European Public Assessment Reports	13 (10%) clinically superior
Lexchin, 2012[29]	2004-2009	Canada, US, France	136 TPD decisions, 145 FDA decisions, 12 HDAP decisions, 624 Prescrire ratings	TPD (priority review), FDA (priority review), HDAP evaluations, Prescrire ratings	TPD: priority reviews to 46 of 137 products (34%) FDA: priority review to 71 of 145 drugs (49%) HDAP: innovative drugs 12 of 120 (10%) Prescrire: innovative new drugs and new indications for older drugs 49 of 624 (8%)

Vitry et al, 2013[30]	2005-2007	Australia	217 Therapeutics Goods Administration approvals (59 drug indications with therapeutic value assessment included)	Authors based on Motola's and Ahlqvist-Rastad's rating systems	Motola's rating system (out of 59 drugs): 31 (53%) pharmacological/technological innovations 4 (7%) modest innovations 17 (29%) moderate innovations 7 (12%) important innovations Ahlqvist-Rastad's system (out of 59 drugs): 19 (32%) "added therapeutic value" 25 (42%) "similar therapeutic value" 5 (8%) "inferior therapeutic value" 10 (17%) "uncertain therapeutic value"
Lexchin, 2018[31]	1995-2016	Canada	623 drugs approved by Health Canada	Health Canada pathways/ evaluations	185 of 623 drugs (29.7%) through an expedited pathway 55 of 509 (10.8%) drugs with therapeutic evaluations as therapeutically innovative
Rodwin, 2020[32]	2009-2016	France	680 drugs evaluated by HAS	ASMR ratings	No clinical improvement 51% (ASMR V) Minor improvement 22% (ASMR IV) Moderate improvement 8% (ASMR III) Important improvement 3% (ASMR II) Major improvement 1% (AMSR I)

Kergall et al, 2021[33]	2014-2020	France	132 drugs evaluated by HAS	ASMR ratings	No clinical improvement 23% (ASMR V) Minor improvement 40% (ASMR IV) Moderate improvement 31% (ASMR III) Important improvement 6% (ASMR II) Major improvement 0% (AMSR I)
Rodwin et al, 2021[34]	2004-2017	France	36 drugs (68 cancer indications) evaluated by HAS	ASMR ratings	No clinical improvement 32% (ASMR V) Minor improvement 38% (ASMR IV) Moderate improvement 22% (ASMR III) Important improvement 7% (ASMR II) Major improvement 0% (AMSR I)
Wieseler et al, 2019[35]	2011-2017	Germany	216 drug-indication pairs evaluated by the IQWiG	IQWiG ratings	Less benefit 1% Non-quantifiable benefit 7% No added benefit 58% Minor added benefit 9% Considerable added benefit 15% Major added benefit 10%
IQWiG, 2022[36]	2011-2021	Germany	20 drugs (41 rare disease indications) evaluated by IQWiG	IQWiG ratings	Less benefit Non-quantifiable benefit 15% No added benefit 54% Minor 7% Considerable added benefit 22% Major added benefit 2%

KCE, 2022[37]	2004-2017	Belgium	40 oncology drugs (12 cancer indications); these drugs were some of the most commonly used and/or the ones with the highest annual expenditure	Authors based on observational data, the medical literature and UK economic evaluations	6 indications: minor improvements in survival 6 indications: no positive evolution in survival Impact on quality of life very uncertain

Notes: FDA, Food and Drug Administration; CPMPRB, Canadian Patented Medicine Prices Review Board appraisals; EMA, European Medicines Agency; TPC, Therapeutic Products Directorate; HDAP, Human Drug Advisory Panel; HAS, Haute Autorité de Santé; ASMR, Amélioration du Service Médical Rendu; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen.

513 **Table 2:** Recommended government actions for the promotion of medically valuable
514 innovation along the lifecycle of new medicines
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Mechanisms	Medicine lifecycle stages	Examples
Patent system reform in alignment with drugs' therapeutic value prospects or patents abolition and use of outcome-based rewards	Discovery and preclinical research	More stringent or downstream patent awards (e.g. based on mechanism of action or following preclinical research); advanced market commitments to purchase drugs at pre-agreed price and volume
Communication of needs-focused R&D priorities in alignment with unmet medical needs by public health authorities	Discovery preclinical research, early clinical development	"Health needs-based" target product profiles outlining desired characteristics or attributes of target products
Allocation of public research funds with a stake in resulting intellectual property	Preclinical research	Retention of ownership by public funders leveraged for reduced product prices
Raising evidence requirements for market authorisation	Licensing	Requirement of comparative clinical trials against existing treatments
Pricing and reimbursement policies in alignment with drugs' value	Post-licensing	Comparative clinical effectiveness and cost-effectiveness

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