High drug prices and the adequacy of return on public investment into drug research and development by the U.S. National Institutes of Health (NIH).

Jarosławski S[1], Toumi M[1,2], Auquier P[2], Borissov B[3], Dussart C[4]

[1]Aix-Marseille University, Marseille, France; [2]Creativ-Ceutical, Paris, France; [3]Prescriptia EOOD, Sofia, Bulgaria, [4]Lyon 1 University, Lyon, France

BACKGROUND

In 2018, the US National Institutes of Health (NIH) spent $34 billion of taxpayer money to support research. NIH was directly or indirectly associated with all 210 new molecular entities (NMEs) approved by the FDA from 2010 to 2018. NIH's mission is to benefit the public health, but also to provide a financial return on public investment. Some of the most expensive drugs approved to date originated, via technology transfer agreements, from NIH's sponsored research.

OBJECTIVES

We discuss the adequacy of return on public investment into drug research and development (R&D).

METHODS

Literature review.

RESULTS

NIH contribution to drug research and development

- In FY 2018, the National Institutes of Health (NIH) had a budget of more than $34 billion to spend on medical research [1].
- Some of the research translates into early-stage products that are later licensed to companies which develop them further in order to obtain FDA approval and then earn billions in sales. Also, NIH research translates into early-stage products indirectly, by generating scientific knowledge and innovations that aid in pharmaceutical development.
- Studies showed that about 9% of the new drugs approved by FDA were based on a patent held by either a government agency or a nongovernmental institution that had received government support [2] or were discovered in public sector research institutions [3]. However, 46.2% of new-drug applications that originated from the public sector research institutions received the FDA's consideration of the highest potential therapeutic effect, as compared with 20.0% of applications for the private-sector originated molecules [3].
- Further, when the direct and indirect effect of NIH funding is considered, **NIH was "directly or indirectly associated with all 210 new molecular entities (NMEs) approved by the FDA from 2010 to 2018** [4]. The indirect contribution originates from a "spill-over" effects of research in basic sciences which does not lead to patents and licensed. Further, NIH investments in a particular research area have been shown to increase subsequent private sector patenting in that area [5].

The adequacy of returns on public investment into drug research by NIH

- NIH's stated mission is to benefit the public health, but also to provide a financial return on public investment [1]. The financial return is obtained via royalty fees collected by NIH mostly from the sales of commercialized products based on licensed technologies. Public R&D spending, especially for basic research, can increase the level of country's GDP and also the potential economic growth [6]. However, in this paper, we will focus on the financial returns which are stated in the NIH's mission.
- In the current scenario, the **NIH obtains its return on investment (ROI) via royalties linked to the sales of commercialized products.** Therefore, high prices of these drugs translate into higher revenues for the NIH. These revenues can be reinvested by the Institutes to fund new research.

Royalty payments vs. commercial drug sale revenues.

- NIH's royalties from licensing agreements have amounted to over $100 million yearly since 2012 [7]. However, data on royalties obtained by NIH for individual products is not available publicly.
- According to data published by the NIH since 2004, Merck's recombinant human papillomavirus vaccine to protect against cervical cancer and Takeda's bortezomib for multiple myeloma have been among the top royalty-generating products. In 2018, the vaccine's worldwide sales topped $3.15 billion and continue to increase [11] whereas bortezomib recorded peak sales at above $2 billion [12].
- Janssen's duranavir, a second-generation protease inhibitor for the treatment of HIV-1 patients, topped the 2017 list of NIH's best royalty revenue generators. In 2018, the drug's worldwide sales neared $2 billion [13].
- Spark Therapeutics' voretigene neparvovec for the treatment of Leber's congenital amaurosis (blindness) was priced at $850,000 per patient and Novartis' tisagenlecleucel for treatment for B-cell acute lymphoblastic leukemia was priced at $475,000 per treatment [14].
- As shown above, the **NIH's total yearly royalty revenue from all its inventions is orders of magnitude less than commercial sales of a single drug.**

Royalty payments vs. NIH's investment.

- Since the product royalties received by the NIH are in the range of $100 million yearly and the annual budget exceeds $30 billion, the royalties compromise merely 0.3-0.4% of the NIH's spending.
- Because the time from R&D investment to commercial licensing is usually in the range from several years to decades, this represents a negative return on investment due to inflation.
- ROI of 9.5% and above is considered financially viable for investors [16].
- In a time-series analysis of US data from 1930 to 2015, investments in the pharmaceutical industry were shown to be 14% compared with 11% for the broader stock market [17]. Further, risk-adjusted returns of this industry were still above the general market [17].
- Using the most conservative ROI value of 9.5%, **the NIH's return from royalties would need to increase 24 fold in order to bring it in line with the financial market returns.**

Possible solutions for improving NIH's return on investment

- Increasing the financial ROI can only be achieved by increasing the royalty payments by the licensees to the NIH. Given the high prices of recently approved drugs, such increase could be achieved by **increasing the NIH's share in commercial sales of the products.**
- The American public who funds NIH via taxes later has to bear the often-high costs of the drugs via insurance premiums and on the top of out-of-pocket payments. In fact, like other licensors, NIH is not allowed to control the prices of these drugs because of the antitrust law [18]. Therefore, increasing financial ROI to taxpayers could be achieved **by reducing the prices of drugs that originate from NIH's investment into R&D.**
- In countries with single, publicly-funded health payer, the **governments step in to negotiate prices of drugs deemed too expensive**, especially in cases when those have been developed using public funds. For instance, the Italian drug pricing committee argued that strimvelis for the treatment of severe combined immunodeficiency due to adenosine deaminase deficiency (ADA SCID) was developed with a financial contribution from regional charities. As a result, **GlaxoSmithKline had to halve its initial pricing bid** and agreed to price the drug at $665,000 per treatment.
- However, rather than improving the transparency of drug pricing in the US, the current US policy aims at incentivizing the US industry to reduce drug prices, e.g. by pressurizing foreign countries to increase the prices of US drugs via bilateral trade negotiations [19,20]. However, it remains to be seen in drug prices in the US drop, even if the prices abroad increase.
- Another way to increase the NIH's ROI for American taxpayers would be to impose a **1% tax on pharmaceutical companies' turnover in the US**. This would represent around 3.5$ Billion annually, which, if reinjected, could cover slightly above 10% of the NIH's yearly budget.
- However, the Trump administration has been similarly opposed to taxation, an emblematic case being the reduction of the corporate tax rate from 35% to 21% in 2017. As such, his administration is unlikely to impose a novel tax on pharmaceutical firms, even if it is of only 1%
- To the extent that NIH research contributes to a majority of pharmaceutical innovations, and given the NIH's weak annual ROI, one may think its role resembles **indirect State aid to private firms.**
- A similar case was that of the Boeing-Airbus trade row, in which the EU alleged that Boeing benefited from access to research and "valuable patent rights" from NASA and the Department of Defense (both publicly funded). The NIH arguably provides similar advantages to pharmaceutical firms, which (once proven) does fit the definition of Subsidies given by the WTO, either as a "government revenue that is otherwise due [which] is forgone or not collected" or as the government providing "goods or services"

CONCLUSIONS

- NIH-funded research has been directly or indirectly responsible for virtually all drugs approved by the FDA in recent years [4].
- Further, twice as many drugs originating directly from NIH-funded projects were highly innovative, compared to drugs from commercially-funded R&D [3].
- However, the American public pays twofold for the medical innovation that is available to them: by financing medical R&D through NIH grants and by purchasing health insurance premiums and out-of-pocket drug spending.
- Overall, the financial ROI on NIH-funded research to the taxpayers seems to be inadequate. The returns to the public could be increased directly by increasing NIH's share in commercial sales of licensed products or indirectly by reducing the prices of the drugs that originated from NIH-funded research.

REFERENCES

1. NIH Technology Transfer FY-18 Annual Report. 2019, NIH
2. Sampat, B Health Affairs, 2011. 30(2): p. 332-339.
3. Stevens, AJ et al. NEJM, 2011. 364(6): p. 535-541.
4. Galkina CE., et al., PNAS, 2018. 115(10): p. 2329-2334.
5. Azoulay, P., et al.The Review of Economic Studies, 2018. 86(1)
6. Fournier, JM., The Positive Effect of Public Investment on Potential Growth. 2016.
7. NIH Royalty Income www.ott.nih.gov/tt-metrics/royalty-income.
8. Young, B Public Citizen Congress Watch.
9. NIH Contributions to Pharmaceutical Development, 200, NIH
10. Druss, B., et al., Health Affairs, 2004. 23(5): p. 210-216.
11. Merck's Gardasil blockbuster sales prompt $1B plant expansion.
12. Penndorf, D., Neural Regen Res, 2018. 13(2): p. 173-180.
13. Johnson & Johnson Reports 2018 Fourth-Quarter Results
14. What a Year It Was! A Look Back at Research Progress in 2017. National Institutes of Health, 2018.
15. JB, K. Taxpayer Funded Development of Truvada as PrEP. 2018 Available from: https://breakthepatent.org
16. Scannell, J.WRev Recent Clin Trials, 2015. 10(1): p. 28-43.
17. Thakor, R.T., et al., Nat Biotechnol, 2017. 35(12): p. 1149-1157.
18. Jarosławski, S., et al., Pharm Res, 2018. 35(3): p. 52.
19 American Patients First. 2018 06/06/2019]; Available from: https://www.hhs.gov/sites/default/files/AmericanPatientsFirst.pdf.
20. Trump threatens to use US trade talks to force NHS to pay more for drugs 2019 06/06/2019]; Available from: https://www.telegraph.co.uk/news/2018/05/15/trump-threatens-use-us-trade-talks-force-nhs-pay-drugs/

ISPOR 2019, Copenhagen, Denmark, November 2-6 2019. PMU9.