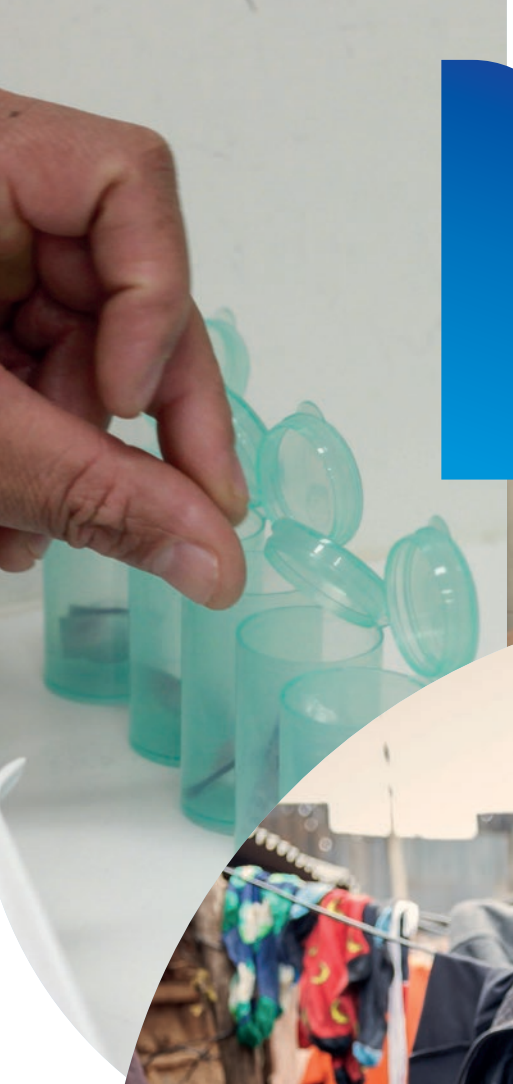

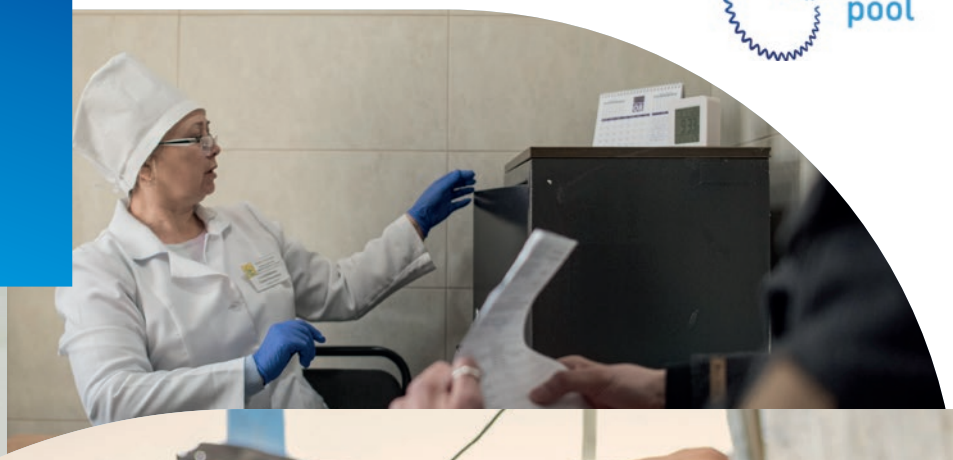

medicines patent pool

VOLUNTARY LICENSING

RIGHT FOR HEALTH SMART FOR BUSINESS

How voluntary licensing advances global health while being economically viable for biopharmaceutical companies.[1]

APRIL 2024

1. Biopharmaceutical companies include all pharmaceutical companies focusing on the research, development and production of both biologic drugs and the more traditional chemically synthesized molecules.

ACRONYMS

CSR Corporate Social Responsibility
ESG Environmental, Social and Governance
FDA Food and Drug Administration
GMP Good Manufacturing Practice
HE Health Equity
HIV Human Immunodeficiency Virus
IP Intellectual property
LMICs Lower Middle-Income Countries
MPP Medicines Patent Pool
NCDs Non-Communicable Diseases
NGO Non-Governmental Organisation
NRA National Regulatory Agencies
R&D Research and Development
SDG Social Development Goals
SLBs Sustainability Linked Bonds
SRA Stringent Regulatory Authority
UMICs Upper Middle-Income Countries

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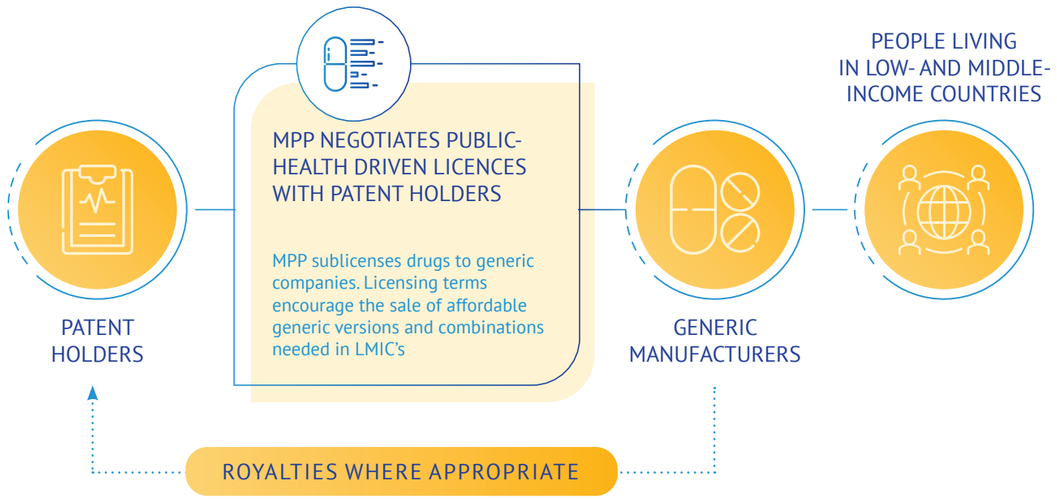
ABOUT THE MEDICINES PATENT POOL

The Medicines Patent Pool is a United Nations-backed public health organisation working to increase access to and facilitate the development of life-saving medicines for low- and middle-income countries. Through its innovative business model, MPP partners with civil society, governments, international organisations, industry, patient groups, and other stakeholders to prioritise and license needed medicines and pool intellectual property to encourage generic manufacture and the development of new formulations. As of April 2024, MPP has signed agreements with 22 patent holders for 13 HIV antiretrovirals, one HIV technology platform, three hepatitis C direct-acting antivirals, a tuberculosis treatment, a cancer treatment, a post-partum haemorrhage prevention medicine, four long-acting technologies, three oral antiviral treatments for COVID-19 and 16 COVID-19 technologies. MPP was founded by Unitaid, which continues to be MPP's main funder. MPP's work on access to essential medicines is also funded by the Swiss Agency for Development and Cooperation (SDC). MPP's activities in COVID-19 are undertaken with the financial support of the Japanese Government, the French Ministry for Europe and Foreign Affairs, the German Agency for International Cooperation and SDC.

THE MPP MODEL – HOW WE WORK



FOREWORD

Dear readers,

Equitable access is a widely accepted goal, but we are still far from achieving it. The fine words, the bold commitments, the unprecedented focus – they are wonderful. But what we need is to turn them into concrete results that see billions more people really reaping the benefits.

Clearly, biopharmaceutical companies, as innovators and producers of life-saving medicines, hold one of the keys to advancing global health equity. Over the years companies have tried a number of different approaches, such as donations, tiered pricing, bilateral commercial licensing and non-exclusive public health voluntary licensing.

Our contention is that non-exclusive public health licensing, despite its success in certain therapeutic areas such as HIV, has been hugely underutilised. This is partly due to misplaced concerns about its risk, partly due to misunderstandings about how it works and how flexible it is and partly due a misconception that it is simply a philanthropic activity, which means that it often has little profile or priority within companies.

The intent of this report is to demonstrate that voluntary licensing goes beyond good intentions and philanthropy, that, while not offering huge commercial returns, it can generate non-negligeable commercial benefits, but with no cost and very little risk. Engaging in voluntary licensing agreements with the right partner represents a sustainable way to increase access while yielding commercial returns for originators.

Voluntary licensing can be both right for health and smart for business. It is time to change perceptions and to grasp all the opportunities that voluntary licensing offers.

Yours truly,

Charles Gore
Executive Director

ACKNOWLEDGEMENTS

This report owes its completion and existence to the generous funding provided by the Government of Canada and the World Intellectual Property Organization (WIPO), whose commitment to advancing the understanding of voluntary licensing has been unwavering.

Equally, the guidance and insightful feedback offered by the members of the Advisory Board have been instrumental in pressure-testing and refining the structure, content, and the language of this report. The Advisory Board gathered representatives of the Bill & Melinda Gates Foundation; the Global Fund; the IFPMA (International Federation of Pharmaceutical Manufacturers & Associations); the JPMA (Japan Pharmaceutical Manufacturers' Association) and WIPO. The content and views expressed in this report do not necessarily reflect the position of individual Advisory Board members, nor the organizations or companies they represent, or those which are cited in this report. We are profoundly grateful for the Advisory Board's insights and are honoured to have had the opportunity to interview each of them.

Disclaimer: The views expressed in this report are those of the authors and not of the funders or Advisory Board members.

ANALYSIS

MPP partnered with the Boston Consulting Group (BCG) to conduct this study aimed at demonstrating the value of voluntary licensing.

Research was conducted using quantitative and qualitative data. The quantitative data used for the analyses was collected from IQVIA (2020-2022 IQVIA MIDAS & IQVIA data request) and from the MPP database. The analyses were conducted on 22 low- and middle-income countries: 11 of these are LMICs: Algeria, Bangladesh, Egypt, India, Jordan, Lebanon, Morocco, Pakistan, Sri Lanka, Tunisia, Vietnam, and 11 are UMICs: Argentina, Brazil, China, Colombia, Indonesia, Malaysia, Mexico, Russia, South Africa, Thailand, and Turkey. Analyses are based on selected real molecule sales and were restricted by data availability as some datapoints are difficult to come by, especially on vaccines. The analyses contain almost no modelling. When projections are used, which is rare, it is explicitly mentioned.

To complement the quantitative data, interviews with nine global access experts and five human resources experts from leading biopharmaceutical companies were conducted with the aim of gaining deeper insight on the level of operational costs linked to licensing implementation.

EXECUTIVE SUMMARY

Voluntary licensing is one of several approaches that has been proven to help expand access to medicines. **If done in the right conditions, use of voluntary licensing for medicines and vaccines could increase patient reach for biopharmaceutical companies and could contribute to reducing global health inequalities, while being economically viable.**

THERE IS AN OPPORTUNITY FOR VOLUNTARY LICENSING ON NCDs

While many of the highest-profile voluntary licences have been for infectious diseases such as HIV and HCV, as well as the COVID-19, **there is an opportunity for voluntary licensing within NCDs.** NCDs account for 74% of all deaths globally, 77% of which are in low- and middle-income countries and include mainly diabetes, cancer, and cardiovascular and respiratory diseases. These are explored in the analysis of this report.

REPRESENTING COMMERCIAL BENEFITS FOR ORIGINATORS

There exists a market for both originator and non-originator product sales in low- and middle-income countries. Indeed, non-originator sales of molecules treating diabetes, oncology, and cardiovascular diseases across 22 LMICs and UMICs represent **between 6% and 28% of market share in value** depending on the therapeutic area.

Contracting licensing agreements can allow originators to leverage manufacturers' margin levels in UMICs and open revenue streams by negotiating margin splits. Therefore, voluntary licensing could unlock between **2% and 17% of additional revenue for originators in UMICs.**

AND ENABLING TO INCREASE PATIENT REACH

As a whole, non-originator products treating diabetes, oncology, and cardiovascular diseases **reach four times more patients** than originator products do across 22 LMICs and UMICs.

Increasing patient reach and patient diversity with voluntary licensing could allow data collection on a larger patient base, **strengthening Real-World Evidence (RWE) corpus on a licensed product.**

HEALTH EQUITY STRATEGIES HAVE AN IMPACT ON EMPLOYEE RETENTION AND COST OF BORROWING FOR ORIGINATORS

Health equity strategies such as voluntary licensing increase talent attraction and retention and therefore can reduce attrition rates by 1%. This 1% reduction in attrition rate is estimated to save biopharmaceutical companies from USD 7 million to USD 50 million depending on company size, training time and average salaries.

Strategies such as voluntary licensing that improve access to healthcare products for priority diseases and in priority countries represent sustainability targets that allow biopharmaceutical companies to issue SLBs. These bonds usually have low interest rates and contribute to reducing biopharmaceutical companies' cost of borrowing.

THE BENEFITS OF LICENSING VIA THE MPP

Voluntary licences can be contracted bilaterally between companies and/or via MPP. Both options require a high level of trust, partnership, and investment by both the originator and recipient parties, meaning that they can only be on mutually agreed terms.

MPP's hands-on licence management model can help mitigate product diversion (the unauthorised sales of products outside of the originator's intended geography or intended distribution channels) through (i) trustworthy collaborations with partners; (ii) strict licensee selection processes; (iii) SRA approval requirements prior to and in addition of the needed regulatory approval in each individual country; (iv) post-market surveillance mechanisms; (v) stringent trade dress requirements; and (vi) strong legal frameworks.

MPP's approach to mitigate product diversion can prevent originators from **yearly revenue loss estimated to range between USD 2 million per LMIC and USD 8 million per UMIC.**

Annual operational costs associated with bilateral agreements are estimated to reach USD 10 million in consultancies and partnership management fees to license one product in 22 LMICs and UMICs. These licence management costs are completely avoided with MPP as a partner.

VOLUNTARY LICENSING, AN ACCESS STRATEGY AMONG OTHERS

Finally, it should be recognised that voluntary licensing alone is not sufficient to ensure patient access to all medicines – healthcare system capability to diagnose patients and deliver treatments are critical, together with other key capabilities along the regulatory and supply chains, including raw materials sourcing, cold chains, tariffs, and export restrictions. Finally, political commitment and government funding to invest in health are key to enabling access to medicines.

INTRODUCTION

The COVID-19 pandemic highlighted the relevance of trust in the biopharmaceutical industry, the need to build a resilient healthcare system and the importance of equity in access to medical products. Indeed, half of the population living in low- and middle-income countries still lack adequate access to essential medicines, vaccines, and other critical health tools.

Stakeholders have been increasingly expecting biopharmaceutical companies to "give back" to society and to tackle health inequities on a global scale. By adopting more integrated global access strategies, biopharmaceutical companies can address these market expectations and show social responsibility which contributes to preserving their brand and reputation. According to KPMG & Lloyds, corporate brand and reputation account for 39% of the market capitalization of the healthcare industry[2].

Inequitable access to medicines is most pronounced in the sphere of innovative pharmaceutical products treating diseases of public health importance which are typically subject to IP protection. Yet, as was demonstrated during the COVID-19 pandemic, IP systems can play a critical role in incentivising innovation and rapid product development of safe and effective medical treatments and sustainable access to quality medicines is achieved by creating the necessary incentives for medicines innovation.

Voluntary licences are contracts entered freely into by IP holders and by generic manufacturers, in which the former authorise the latter to manufacture patented products and sell them in specified low- and middle-income countries. Sharing IP in low- and middle-income countries through voluntary licences is one of the industry-led access strategies and is embraced as a solution to increase access to innovative products at affordable prices and to scale up local generic manufacturing in these countries in the context where governments are now strongly focused on local manufacturing to overcome the severe impacts of disrupted global chains, increasingly requiring providers to be locally based.

Companies such as Gilead, ViiV Healthcare, AbbVie, Merck, Janssen and BMS have been involved in licensing in disease areas such as HIV to generic manufacturers for nearly two decades, enabling millions of HIV patients around the world to access the medicines they need. Yet, voluntary licensing has not been used as much as it could be.

Two main voluntary licensing models exist and can be selected depending on market conditions, countries' needs and originators' motivations with licensing.

One of the licensing models is a direct licence management model by which originators contract licences themselves through bilateral agreements with one or more generic manufacturers. In some cases, biopharmaceutical companies that have existing operating models in low- and middle-income countries choose to license only a part of the value chain.

The other model is the indirect licence management model, one in which originators license their IP to a third party such as MPP to sub-license on their behalf, according to a pre-agreed set of criteria and standards. Typically, MPP negotiates licence agreements with originators including the financial terms and sub-licence agreements and then issues sub-licences to multiple generic licensees for sale into pre-defined countries. These different models will be discussed and compared in part 2 of the report.

The primary purpose of voluntary licensing is to reduce global health inequity by increasing the availability of pharmaceutical products to populations living in low- and middle-income countries. The analysis in this report focuses on the value of the voluntary licensing model for medicines, but voluntary licensing is also relevant for vaccines, as demonstrated by licensing agreements signed during the COVID-19 pandemic. Because vaccines are complex and cannot be easily copied with a licence on a patent, successful voluntary licences in this space are usually coupled with technology transfer, know-how, and other technical assistance. The mRNA technology transfer Programme, a global initiative co-led by MPP initially focusing on mRNA vaccines against COVID-19 was designed to equip partners in low- and middle-income countries across the world with training, technology development and technology transfer to produce and sell mRNA vaccines. Such initiatives contribute to paving the way for successful future voluntary licensing agreements on vaccines by putting in place the necessary competencies and capacity to receive the technology.

Jeremy Farrar, Chief Scientist at the World Health Organization: "*Vaccine supplies aren't yet enough (...) We have to look at supply chains and where we manufacture vaccines. This isn't just a problem for Europe: there's little manufacturing in Africa, parts of Asia, and central and South America. We'll need technology transfer. Voluntary licensing will be part of the solution*[3]*". "We should make vaccines broadly available. it is enlightened self-interest: not only from a public health perspective but also for biopharmaceutical companies.*[4]*"*

"Vaccine supplies aren't yet enough (...) We have to look at supply chains and where we manufacture vaccines. This isn't just a problem for Europe: there's little manufacturing in Africa, parts of Asia, and central and South America. We'll need technology transfer. Voluntary licensing will be part of the solution".

Jeremy Farrar, Chief Scientist at the WHO

2. KPMG & Lloyds. (2020). Safeguarding reputation. Retrieved from: https://assets.lloyds.com/assets/safeguarding-reputation/1/Safeguarding%20reputation.pdf

3. BMJ (2021). Jeremy Farrar, make vaccines available to other countries as soon as our most vulnerable people have received it. Retrieved from: https://www.bmj.com/content/372/bmj.n459

4. BMJ (2021). Jeremy Farrar, it's self-interest to share our vaccines globally. Retrieved from: https://doi.org/10.1136/bmj.n536

PART 1 - WHY IS VOLUNTARY LICENSING INTERESTING FOR BIOPHARMACEUTICALS?

The objective of part 1 is to provide evidence that voluntary licensing can lead to an increase in the number of patients treated in low- and middle-income countries whilst generating revenue for biopharmaceutical companies. The analyses in the following sections were conducted using real sales data from IQVIA and from the MPP database on 22 countries: 11 UMICs[5] and 11 LMICs[6]. Non-originator sales include products that have been licensed (both voluntary & compulsory licensing) and products that are off-patent.

5. Argentina, Brazil, China, Colombia, Indonesia, Malaysia, Mexico, Russia, South Africa, Thailand, Turkey.
6. Algeria, Bangladesh, Egypt, India, Jordan, Lebanon, Morocco, Pakistan, Sri Lanka, Vietnam, Tunisia

I. VOLUNTARY LICENSING HELPS EXPAND PATIENT REACH.

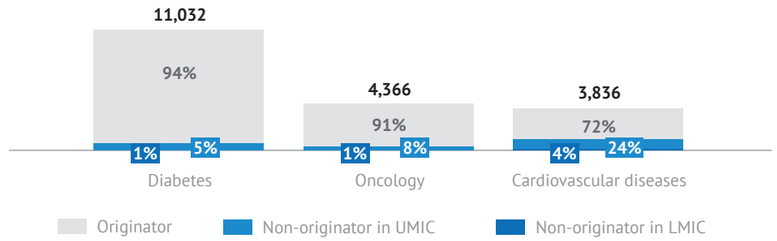
Analysis #1 – Non-originator vs. originator product sales

One of the reasons biopharmaceutical companies are reluctant to enter in voluntary licensing agreements is the misconception that there is a very small market for non-originator products (both licensed and off-patent) in low- and middle-income countries.

However, analysis of originator and non-originator sales of molecules treating the NCDs diabetes, oncology, and cardiovascular diseases across 22 LMICs and UMICs reveal that non-originator sales represent **between 6% and 28%** of total product sales in value depending on the therapeutic area. Therefore, on average, 11% of product sales by value are generated by non-originators. **This demonstrates that there is a market for non-originator products in LMICS and UMICs and that the originator market does not capture all of the demand in these countries.** The data also shows non-originator sales are driven by China, India, Russia, Brazil, Argentina, and Thailand; nonetheless smaller markets still represent approximately 3% of sales.

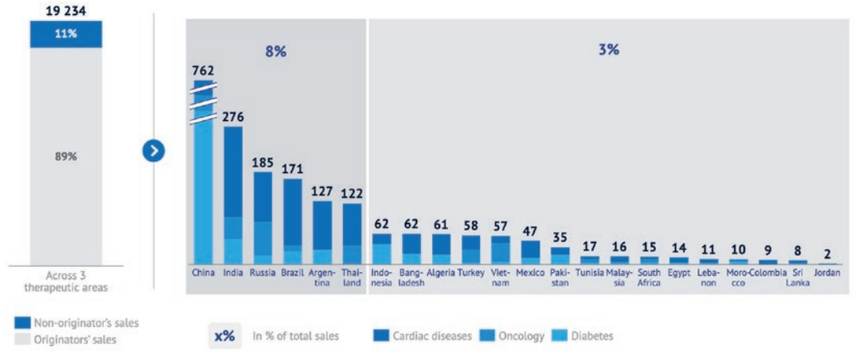
ANALYSIS 1 - Non-originator vs.originator sales

FIGURE 1 - Non-originators' sales constitute 6% to 28% of total sales per therapeutic area



Average molecule sales in USD million, split between originators and non-originators

FIGURE 2 - Within our sample non-originators' sales are driven by China, India, Russia, Brazil, Argentina & Thailand; smaller markets still represent ~3% of sales



In USD million, average sales for 2020, 2021, and 2022. Source: IQVIA MIDAS Oct. 2023 in 22 countries

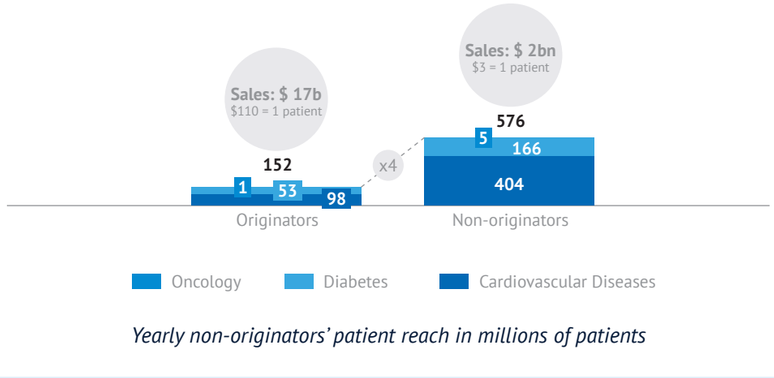
Representativity: Large sample
Data source: IQVIA MIDAS; extracted October 2023
Geographies: 22 countries
Timeframe: 2020 to 2022
TA: Diabetes; Oncology; Cardiovascular Diseases
Molecules: Atovarstatin; Bosentan; Fulvestrant; Glimepiride; Imatinib; Insulin Glargine; Metoprolol; Repaglinide; Trastuzumab (please see 'country data per molecule' in appendix for detail)
Methodology:
1. Identify originators vs. non-originators' products
2. Calculate sales for both per molecule and per country
3. Calculate the average for 2020, 2021, 2022

Analysis #2 – Non-originator vs. originator patient reach

Potential patient reach is disproportionate to the value of product sales: patient reach can be drastically improved with more affordable products. To estimate patient reach for both originator and non-originator products, data on product packs sold was collected in each country. Then the total number of product packs sold was divided by the estimated yearly consumption per patient in each country. The results show that between 2020 and 2022, non-originator products reached on average **576 million patients yearly** whereas originator products reached **152 million patients yearly.**

ANALYSIS 2 - Non-originator vs.originator patient reach

FIGURE 3 - Though non-originators represent only 11% of molecule sales; they reach x4 more patients



Representativity: Large sample
Data source: IQVIA MIDAS extracted October 2023; European Medicines Agency; Base de données publique des medicaments (FR); Vidal
Geographies: 22 countries (please see 'country data per molecule' for detail)
Timeframe: 2020 to 2022
TA: Diabetes; Oncology; Cardiovascular Diseases
Molecules: Atovarstatin; Bosentan; Fulvestrant; Glimepiride; Imatinib; Insulin Glargine; Metoprolol; Repaglinide; Trastuzumab

Methodology:
1. For each molecule, calculate a conservative yearly consumption of medicine boxes per patient
2. For non-originators and originators, divide the average number of sold boxes in each country with the yearly patient consumption
3. Compute the patient reach per therapeutic area for UMICs & LMICs & in total
4. Compare the difference between licensee's and originator's total

In conclusion, while non-originator (licensed and off-patent) sales represent **11% of product sales in value, they reach 4 times more patients.** This indicates that (i) **there is a significant market for non-originator products in LMICs and UMICs; (ii) by addressing the non-originator market, voluntary licensing allows biopharmaceutical companies to increase patient reach. This is true for medicines and for vaccines.** As Doctor Drew Weissman, who received the 2023 Nobel Prize for his contributions to RNA biology, explains *"mRNA vaccines are fit for most countries: you can do that anywhere. You don't need fancy equipment, a fancy medical centre (...). With voluntary licensing you can drastically scale patient reach."*

"mRNA vaccines are fit for most countries: you can do that anywhere. You don't need fancy equipment, a fancy medical centre (...). With voluntary licensing you can drastically scale patient reach."

Dr. Drew Weissman, 2023 Nobel Prize for his contributions to RNA biology

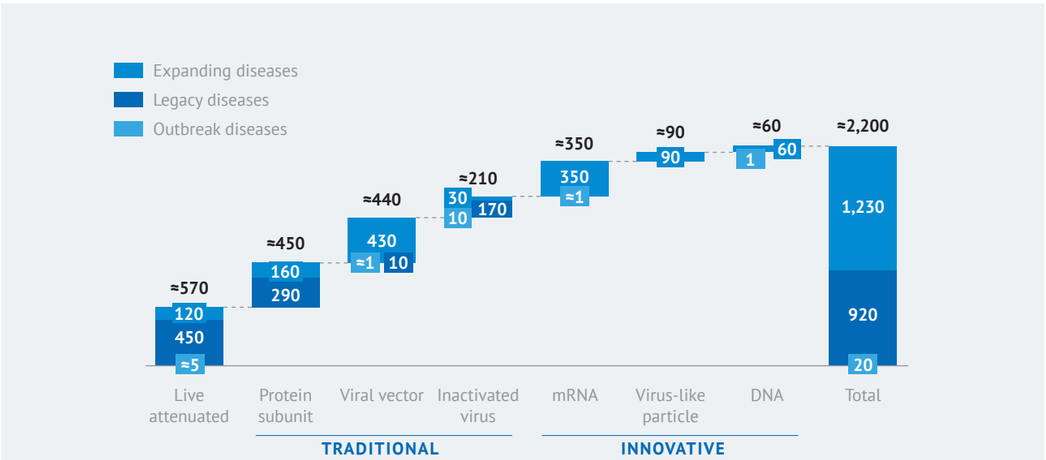
Moreover, the COVID-19 pandemic has caused a fundamental change in the global pharmaceutical industry's operations, with governments renewing their focus on local manufacturing to overcome the severe impacts of disrupted global supply chains. Voluntary licences help advance localisation efforts leading to self-sufficiency, fulfilling domestic needs and empowering national healthcare systems.

During the height of the COVID-19 pandemic, African countries had difficulty accessing life-saving vaccines due to their reliance on supplies from other countries. Doctor J. Kaseya (Africa CDC Director General) illustrated the situation as follows: *"Africa CDC remains determined that Africa should produce its vaccines and protect the lives of all Africans. The African Union has set a target for the continent to produce 60% of the vaccines needed by 2040.*[7]" It is expected that in the next 15 years, c.25% of vaccines administered in Africa will be innovative ones. There is a strong need to bolster African capabilities in vaccine technology transfer and **voluntary licensing should be considered as a critical option to do so.**

"Africa CDC remains determined that Africa should produce its vaccines and protect the lives of all Africans. The African Union has set a target for the continent to produce 60% of the vaccines needed by 2040."

Dr. Jean Kaseya, Africa CDC Director General

FIGURE 4 - Number of vaccine doses administred in Africa by modality (million, 2040)*



*Data only fot the 22 priority Continental Strategy vaccines; assumes that number of doses administred is equal to doses demanded

Source: Linksbridge, Evaluate Pharma; expert interviews

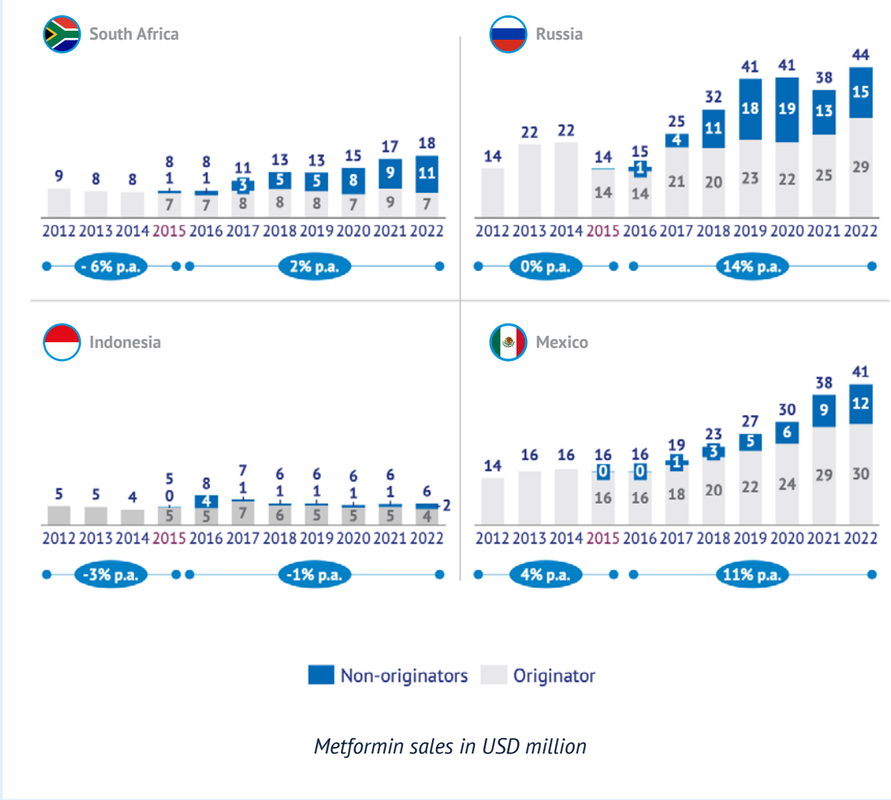
Analysis #3 – Case study showing non-originator sales reach new patient segments

The objective of this analysis is to show that non-originator sales do not cannibalise originator sales. Analysis was conducted on metformin sales between 2012 and 2022 in four countries where originators sold the product before non-originators entered the market. The data in these four countries points out that **non-originator sales did not stop originator sales' growth.** For instance, in Mexico, originator metformin sales grew 4% p.a. in value between 2012 and 2015. And after non-originator market penetration of metformin in 2015, **originator sales continued to grow,** reaching 11% p.a. growth. It can be inferred that **non-originator products reached new patient segments,** that licensing **did not cannibalise originator sales and in fact contributed to increasing patient reach for metformin.**

7. Africa CDC (2023). A Breakthrough for the African Vaccine Manufacturing. Retrieved from: https://africacdc.org/news-item/a-breakthrough-for-the-african-vaccine-manufacturing/

ANALYSIS 3 - Patient segments

FIGURE 5 - Metformin non-originators reached a new patient segment previously untapped by originator



Representativity: Case study
Data source: IQVIA data request; October 2023
Geographies: South Africa; Indonesia; Russia; Mexico
Timeframe: 2012 to 2022
TA: Diabetes
Molecules: Metformin

Methodology:
1. Identify a molecule where the originator is presentin a country; and new non-originators enter the market later on
2. Calculate the originator's compound annual growth rate (CAGR) before and after non-originator's entry

Collecting Real-World Evidence data

Increasing patient reach and diversity of patient groups is a burning topic for biopharmaceutical companies because it allows them to **generate Real-World Evidence (RWE).** RWE is data collected from sources outside of traditional clinical trials and comes into play when the latter does not account for the entire patient population for a product. RWE is increasingly considered by National Regulatory Agencies (NRA) to support new medicines approvals[8], following the lead of US FDA.

The FDA will consider lack of diversity of patient groups in clinical trials as a hindrance to new product approvals. This vision has been highlighted in the recent FDA Advancing RWE Program (2022), particularly in the setting of oncology and rare diseases[9]. The FDA implemented this claim when they rejected Eli Lilly and Innovent Biologics' PD-1 inhibitor Tyvyt (sintilimab) submission in 2022 on the grounds of the lack of representativeness in the clinical trial[10]. Indeed, recent evidence shows that one-fifth of therapies approved in recent years have a different metabolic impact on patients based on their ethnicity[11]. This has historically not been considered in clinical trials. As an example, Black Americans comprise only 5% of the patients who participate in oncology clinical trials in the US, when they account for 13% of the US population.

Licensing increases biopharmaceutical companies' patient reach and patient diversity by providing access to medicines to previously unserved patients across continents. Given proactive planning of data collection is in place to ensure data availability, quality, and data protection, the information collected on a larger patient base could strengthen the RWE corpus that can be used to reinforce studies for new indications, extended usage, or coverage decisions of medical products. In developing countries, the infrastructure to collect and assess this data is being deployed and will continue to grow.

II. VOLUNTARY LICENSING OPENS NEW MARKET SEGMENTS FOR BIOPHARMACEUTICALS WITH FOCUSED GEOGRAPHICAL FOOTPRINT.

New manufacturing capabilities

Entering into licensing agreements benefits originator companies that have focused geographical footprint by **opening production capabilities** in countries where they do not have operational capabilities.

Analysis #4 - New revenue streams

Sales of products in combination with margin splits received from licensees could provide originators with a **viable revenue stream.** This is because GMP-approved manufacturers[12] are currently concentrating their efforts on emerging markets and can manufacture generic medicines at a lower cost than originators can, depending on their supply chain. Therefore, by contracting licensing agreements, originators capitalize on manufacturers' competitive pricing. This is especially the case in UMICs and in India where the market volume is substantial, and prices are still relatively high. In cases where originators do not intend to commercialise products in these countries themselves, production increase due to licensing agreements could **open new revenue segments for them while increasing access in price sensitive segments.**

To quantify the top line impact of licensing strategies in UMICs & India for originators, GMP-approved manufacturer sales data in India were used to estimate minimum production costs. The assumptions taken were that (i) manufacturers never set sales prices below their production costs and that (ii) the minimum sales price on the market would be close to the market production cost, assuming a minimum margin. India was used as a benchmark since it is the world's largest manufacturer of high-quality generic treatments, meeting all quality requirements, at the lowest production costs.

Comparing real sales of nine molecules used to treat diabetes, oncology, and cardiovascular diseases in the selected UMICs and the estimated production cost as explained above shows that **non-originator margins potentially range from 46% to 81% on these product sales.**

8. Including the FDA, https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence
9. U.S. Food & Drugs Administration. (2022). Advancing Real-World Evidence Program. Retrieved from https://www.fda.gov/drugs/development-resources/advancing-real-world-evidence-program
10. DENARIÉ, M. E. (2023). LEVERAGING REAL-WORLD DATA TO ESTIMATE RACE AND ETHNICITY REPRESENTATION IN CLINICAL TRIAL DESIGN. RETRIEVED https://www.iqvia.com/library/white-papers/leveraging-real-world-data-to-estimate-race-and-ethnicity-representation-in-clinical-trial-design
11. SAVILL, K. Z., BROWN-BICKERSTAFF, C., HAYS, H., & SWAIN, S. (2022). HOW REAL-WORLD EVIDENCE CAN HELP FILL CLINICAL TRIAL DIVERSITY GAPS. CARDINAL HEALTH. RETRIEVED FROM https://www.cardinalhealth.com/en/services/manufacturer/biopharmaceutical/real-world-evidence-and-insights/resources-for-real-world-evidence-and-insights/how-rwe-can-help-fill-clinical-trial-diversity-gaps.html
12. GMP - Good Manufacturing Practice is the minimum standard that a medicines manufacturer must meet in their production process.

FIGURE 6 - We estimated the cost of producing each molecule in India, looking at only GMP-approved manufacturers with non-increasing prices

Estimation of molecules' production cost in India, with the following methodology:

- *For each molecule, selection of lowest price point from GMP-approved manufacturer*
- *When price increases, exclusion of year before the increase to avoid selecting "dumping price" point*

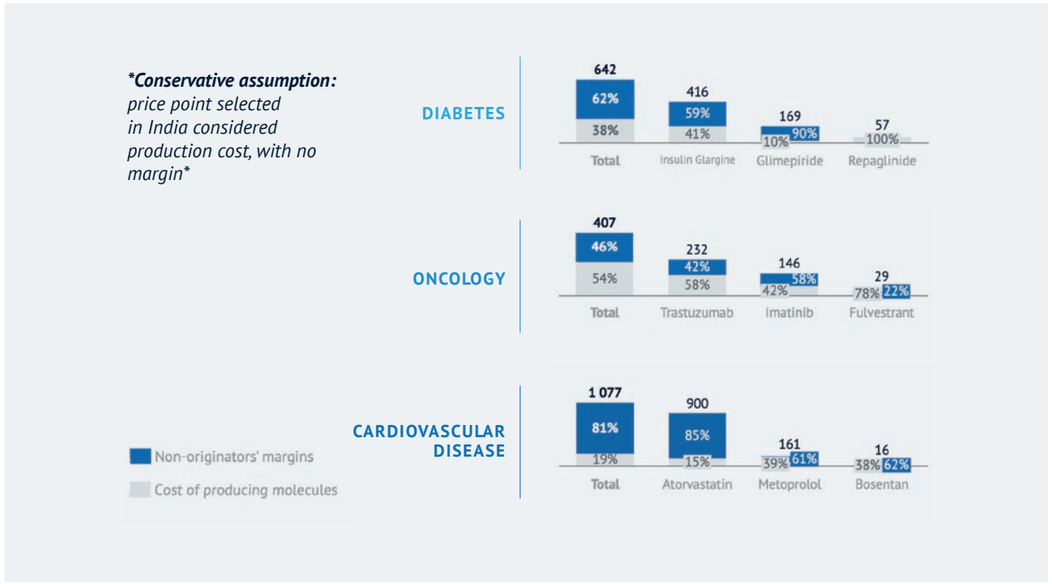
MOLECULE	MANUFACTURER	GMP APPROVED	PRICE FOR 1 UNIT*	OTHER MANUFACTURERS IN 15% PRICE RANGE**
Atorvastatin	Hetero Drugs	✓	US$ 0,02	3% — 31 players under US$ 0.05
Bosentan	Cipla	✓	US$ 0,9	100%
Fulvestrant	Hetero Drugs	✓	US$ 136	20%
Glimepiride	Unison PharmaUS	✓	US$ 0,01	19%
Imatinib	Neon Labs	✓	US$ 0,7	25%
Insulin glargine	Wockhardt	✓	US$ 4,7	50%
Metoprolol	Unison Pharma	✓	US$ 0,02	65%
Repaglinide	Medley Pharma	✓	US$ 0,06	20%
Trastuzumab	Intas	✓	US$ 139,8	0% — Player represents 20% of sales

*Prices in US$ for one standard unit. Average for 2020; 2021; 2022; unless decrease occurred before 2022 – in this case, lower price point before increase was excluded to avoid selecting 'dumping' price point

**Based on most recent (2022) price points

Source: IQVIA MIDAS Oct 2023.

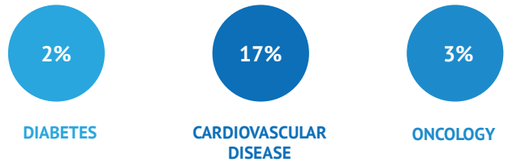
FIGURE 7 - Revenue which comes on top of this production cost ranges from ~50% to ~80%



Contracting licensing agreements can allow originators to leverage manufacturers' margin levels in UMICs & India and open revenue streams by negotiating margin splits. **Indeed, by negotiating the common level 40%/60% of non-originator/originator split on the nine molecule sales in UMICs & India, originators could generate between 2% and 17% additional revenue** (i.e., as shown in figure 1, originator sales make up 72% of the cardiovascular market and by adding a 60% margin split on non-originator sales which represent the 28% of the remaining market, originators could generate an additional 17% of revenue).

ANALYSIS 4 - Additional originator revenue

FIGURE 8 - Additional revenue from implementing royalties in UMICs could range 2% to 17% vs. originator sales



Estimated % of additional revenue for originators in UMICs

Representativity: Large sample
Data source: IQVIA MIDAS; extracted October 2023
Geographies: 22 countries
Timeframe: 2020 to 2022
TA: Diabetes; Oncology; Cardiovascular diseases
Molecule: Atovarstatin; Bosentan; Fulvestrant; Glimepiride; Imatinib; Insulin Glargine; Metoprolol; Repaglinide; Trastuzumab
Methodology:
1. Estimate cost of producing each molecule for non-originators in LMICs & UMICs; taking min. price point in India for GMP manufacturers with stable prices – conservatively assuming no margin
2. Calculate the average for 2020, 2021, 2022.
3. Multiply estimated cost of producing molecules per average volume of sales
4. Apply 60% revenue for originators on difference with cost; in UMICs & India only

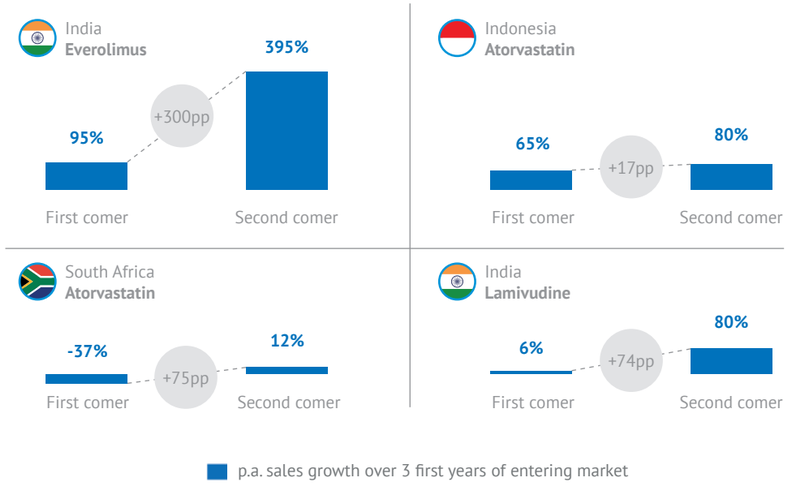
Analysis #5 - Case study comparing first manufacturer vs. second manufacturer USD sales growth

The objective of this case study is to demonstrate that voluntary licensing could advance market shaping and could lead to higher growth for follow-on medicines. External experts' and MPP experts' insights suggest that introducing a medicine in the market could lead to a positive market shaping effect for future medicines. To demonstrate this effect, an analysis was conducted to measure the difference in growth for a follow-on medicine vs. for the first medicine introduced to target the same therapeutic area in three low- and middle-income countries. For this analysis, market shaping is defined as the preparation of a market that facilitates future entry of a follow-on medicine. Preparation of a market includes: (i) advocacy and education of healthcare professionals and affected communities; (ii) government advocacy; (iii) creation of budget lines; (iv) creation of infrastructure to diagnose and treat the disease.

Analysis of sales of three molecules in the oncology, cardiovascular disease and HIV therapeutic areas in India, Indonesia, and South Africa between 2012 and 2022 show that **the sales of the second manufacturer to produce the molecule always grow at a faster rate than sales of the first manufacturer** during the first three years of manufacturing. Indeed, USD sales of products that came later had **an annual growth rate ranging from 17 to 300 percentage points higher** than the sales of the first product. In India and in Indonesia USD sales were 130% to 1200% higher. This could be explained in part by the market shaping capabilities in developing countries, the ease with which infrastructure, manufacturing facilities, supply chain capabilities, healthcare ecosystem can be adapted to sell new products in the future.

ANALYSIS 5 - Market shaping

FIGURE 9 - Second comers' sales grew up to 4x more than first comers in their first 3 years



First comers & second comers' USD sales CAGR over first 3 years of entering market

Representativity: Multiple case studies
Data source: IQVIA data request; October 2023
Geographies: India; Indonesia; South Africa
Timeframe: 2012 to 2022
TA: Oncology; Cardiovascular Diseases; HIV
Molecule: Atorvastatin; Everolimus; Lamivudine

Methodology
1. Identify 2 different manufacturers for the same molecule in the same country, that entered the market at different times
2. Calculate CAGR for the 3 first years of the first to enter market; and the CAGR for the 3 first years of the second to enter market
3. Compare both

PART 1 CONCLUSIONS

- There is an existing market for both originator and non-originator product sales in low- and middle-income countries. **Non-originator sales represent between 6% and 28% of market share depending on the therapeutic area.**
- Non-originator sales reach **four times more patients** than originator sales do.
- Increasing patient reach and patient diversity with voluntary licensing could allow to collect data on a larger and more diverse patient base, strengthening RWE corpus**.**
- For biopharmaceutical companies with focused geographical footprint, **voluntary licensing can unlock between 2% and 17% of additional revenue** in low- and middle-income countries.
- Case studies show that **non-originator sales need not necesserily cannibalise originators sales, particulary if there are different segments, and that low- and middle-income countries have market shaping capabilities** offering opportunities to originators in these markets in the future.

PART 2
-
THE BENEFITS OF VOLUNTARY LICENSING WHEN DONE WITH THE RIGHT PARTNER

I. THE PERCEIVED RISKS OF VOLUNTARY LICENSING

Product diversion

Despite the benefits of voluntary licensing as described in part 1, originator companies recognise the risks that licensing incur for their firms, which can lead them to shy away from this strategy. The main risk identified is product diversion. It refers to the unauthorised sales of products outside of the originator's intended geography or intended distribution channels. This includes the diversion of product sales from licensed countries to high-income countries or products intended to support a public health program diverted and then sold for profit in the private market. Product diversion has a negative economic impact on the overall financing and delivery system of pharmaceutical products. Diverted products are not delivered to the patients for whom they were intended. Moreover, the violation of geographical scope of sale, distribution agreements and IP rights usually involves legal and regulatory issues. Experts agree that product diversion is the main risk associated with licensing: *"It can stem from any step of the licensing value chain. Reliable partners and strong legal binding are vital to curb this issue"*[13].

Quality control

Another perceived risk linked to voluntary licensing is quality control referring to the sales of substandard products. Such products are potentially harmful for patients and, in the case of infectious diseases, can potentially lead to the development of medicine resistance.

These risks can be mitigated by **licensing to trustworthy generic manufacturers** that will adhere to agreed quality-control standards, respect trade dress and will work to prevent product diversion. Moreover, strong contractual terms in licensing agreements should have provisions designed to address concerns over diversion and sales outside of the licensed territory.

Successful licensing agreements are ones by which there is effective coordination and collaboration among all players (licensor, licensee, donors, multilateral organisations, NGOs, and low- and middle-income countries governments) and supply chain efficiency so that generic companies can manufacture the generic medicines.

II. THE MPP INDIRECT LICENCE MANAGEMENT MODEL

Since its inception in 2010, the aim of MPP has been to increase access to and facilitate the development of life-saving medicines for low- and middle-income countries through an innovative approach to voluntary licensing and patent pooling. **MPP's complementary indirect licensing management model** reduces the complexity of navigating distribution chains for originators in countries where they lack presence and expertise and ensures the greatest likelihood that licences will result in significantly enhanced access to medicines[14].

MPP is composed of industry, legal, and public health experts whose licensing work is both upstream (i.e., identification of suitable candidate medicines through prioritisation and development of an enabling environment for in-licensing) **and downstream** (i.e., out-licensing, licence management, technology transfer, and support for access). In-licensing activities have generally started around late product development, regulatory approval, or early market entry. In some cases, in-licensing efforts begin after an approved product is prioritised by a global health mechanism (such as the WHO Model List of Essential Medicines).

As at June 2023, MPP had negotiated and signed agreements with **20 patent holders** and was **managing more than 100 licensed products** in a range of therapeutic areas which have supplied **34.7 billion doses of life-saving treatments in 148 countries.**

There is a great number of entities involved in product distribution such as procurement agencies, importers, distributors, pharmacies, etc.,[15]. Other actors such as the National Medicines Regulatory Authorities (NMRAs), donor governments, funders, NGOs, civil-society organisations are also essential to the operation of voluntary licences. **Over the years, MPP has developed partnerships with many of these entities to ensure trustworthy collaborations with high licensing standards that deliver access on the ground.**

Mitigating quality risk

Prior to any product sales, **MPP requires licensees to seek WHO prequalification or SRA approval before, and in addition to, the needed regulatory approval in each individual country.** Such prequalification or SRA approval helps maintain quality control. MPP also mitigates quality risks by monitoring FDA warnings.

13. BCG interview with global access experts from leading biopharmaceutical companies
14. BMJ global health (2023). Negotiating public-health intellectual property licensing agreements to increase access to health technologies: an insider's story. Retrieved from: https://gh.bmj.com/content/8/9/e012964
15. Harvard et al. (2023) Report of the task force on voluntary licensing and access to medicines. Retrieved from: https://globalaccessaction.org/vlam/.

Moreover, to ensure high quality standards, **MPP carefully identifies generic manufacturers by implementing a rigorous licensee selection process.** This process ensures that licensees have the adequate infrastructure and capabilities to develop the generic product with the same high quality as the originator product. Licensees are also required to have production facilities operating under current GMP, adequate health and safety measures in place, and to have undergone anti-bribery, anti-corruption, trade assessments and export controls. After this identification process, **originator companies have control** over the final approval of the licensees authorized to manufacture their product.

Mitigating product diversion

To mitigate product diversion, MPP has established **effective mechanisms for surveillance after the product is available.** These include reviewing the import and export data to track and monitor the products sold by licensees and flag any suspicious sales. According to MPP licence agreements, all products sold are required to have trade dress, artwork, symbols, or label specifying the territory of sale and hence restricting movement outside territory. In many MPP licences, generic companies are required to seek pre-approval of sales in cases that need particularly stringent oversight.

In 2014, ViiV Healthcare, a global specialist HIV company, began issuing licences to MPP to accelerate access to treatments based on dolutegravir (DTG), a promising new antiretroviral for both adult and paediatric HIV care. In 2016, the two parties extended the adult licence to cover all low- and middle-income countries. By the end of September 2021, the agreements allowed manufacturers to produce generic versions of DTG for at least 95 countries for the adult agreement and 123 countries for the paediatric agreement. According to ViiV Healthcare, 24 million[16] people living with HIV across 128 countries[17] had access to a generic product containing dolutegravir by the end of 2023. Throughout, MPP has been controlling product diversion, monitoring each of the more than 200 million packs sold each year. As an illustration of this, among the 95 countries under the **adult DTG agreement, 13 are royalty-bearing and licensees can access only the public market in these countries (unless direct commercial agreements are in place), and sales by MPP licensees have never unduly reached the private market in these 13 countries.**

Reference pricing

Voluntary licensing to generic manufacturers can help overcome the challenge of external reference pricing that pharmaceutical companies face for their commercial markets in higher-income countries when exploring discounted pricing options for low- and middle-income countries[18]. Indeed, reference pricing, the strategy by which governments consider the price of a product in given countries to derive a reference price in their own country, may not apply to a product made by a different manufacturer and therefore would not apply to a product being supplied by a licensee that has its own market authorization, brand, etc. MPP's licences require that licensees do not use or register any originator trademarks or trade dress on, or in connection with, the licensed products anywhere in the world, including in connection with any sale, distribution, promotion, or marketing of the product. **Therefore, licensing with MPP results in a demonstrably different product, not a second brand that would be under reference pricing constraint.**

III. THE TANGIBLE BENEFITS OF MPP LICENCES.

Analysis #6 – The cost of product diversion

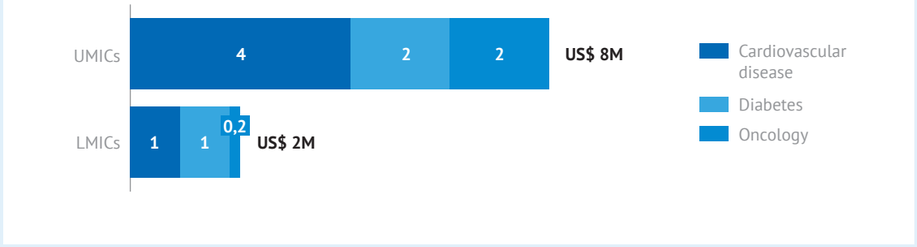
The objective of this section is to quantify the potential costs associated with product diversion which can be avoided by licensing a product with a partner such as MPP. Analysis based on external experts and MPP experts suggests that through its local footprint and expertise and thorough monitoring of licensees, MPP can avoid revenue loss due to product diversion - defined as the illegal diversion of a genuine pharmaceutical product approved and intended for sale in a defined set of countries, but then illegally sold in another country[19].

Interviews with nine global access experts from six leading biopharmaceutical companies[20] with experience in global access in LMICs and UMICs have given an estimate of the yearly product diversion cost in terms of revenue loss in these countries. Assuming their estimates can be replicated to the countries in this study, revenue loss due to product diversion can reach **USD 2 million in yearly revenue in one LMIC and USD 8 million in yearly revenue in one UMIC.** Effective licence management can help mitigate this risk and revenue loss.

16. GSK (Annual Report (2023). Retrieved from: https://www.gsk.com/media/11007/annual-report-2023.pdf
17. GSK (Annual Report (2023). Retrieved from: https://www.gsk.com/media/11007/annual-report-2023.pdf
18. Incze A, Kaló Z, Espín J, et al. Assessing the consequences of external reference pricing for global access to medicines and innovation: economic analysis and policy implications. Front Pharmacol 2022;13:815029.
19. OECD/EUIPO (2020). Trade in Counterfeit Pharmaceutical Products. Retrieved from https://doi.org/10.1787/a7c7e054-en
20. BCG interviews

ANALYSIS 6 - Yearly revenue loss per country due to product diversion cost

FIGURE 10 - Yearly product diversion cost across therapeutic areas in USD million



Representativity: Large sample
Data source: Interviews with nine global access experts from six leading biopharmaceutical companies, IQVIA MIDAS
Geographies: UMICs & LMICs in which experts had experience
Timeframe: 1 year
Product diversion: i) product stolen and sold illegally; ii) product copied to be sold illegally

Methodology
1. Collect experts' estimation of yearly product diversion costs in share of revenue
2. Assume that product diversion costs can be generalized to the scope of our study
3. Calculate the share of revenue loss due to product diversion, based on IQVIA average yearly revenue for each therapeutic area in scope of this analysis

Analysis #7 - Avoiding operational costs

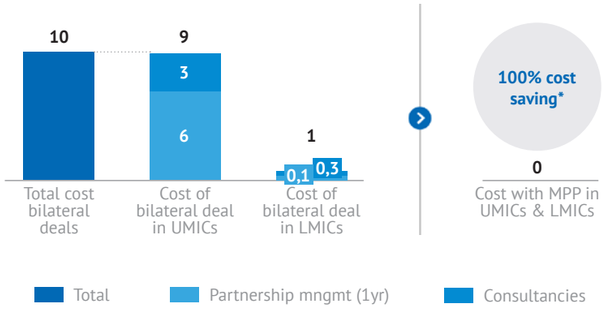
Moreover, direct licence management models by which originator companies negotiate voluntary licences through bilateral agreements themselves implies originators will have to **spend significant time and money** on (i) paid consultants to find the right partners (payments made to intermediaries for market understanding, partnership negotiation) and (ii) management of the licensees (partnership management, manufacturing management, ensuring licensees abide by the terms of the agreement on quality, anti-diversion, geographic coverage, auditing & reporting, etc).

Nine global access experts from six leading biopharmaceutical companies have estimated bilateral licensing annual implementation costs in consultancies and partnership management fees for UMICs and LMICs to reach up to USD 2 million per molecule. Multiplied by the number of necessary processes to enter the 22 countries in this study, considering that seven countries can be entered simultaneously[21], **entering into bilateral agreements for the 22 countries can cost up to USD 10 million annually.** MPP's indirect management model bears these costs for licensors **allowing them to save time and money and to benefit from industry expertise.** Biopharmaceutical companies may choose to dedicate internal business units to the task of managing licences, but MPP's expertise in regulatory dossiers, market knowledge, long-term collaborations and partnerships which foster trust are difficult to compete with. In addition, over the years MPP has used its experience to automate many of the processes, for example trade dress approval or royalty calculation, which both speeds up the process and removes opportunities for human error.

21. Based on experts' input.

ANALYSIS 7 - Annual operational costs

FIGURE 11 - By partnering with MPP, biopharmaceutical companies can avoid 100% of VL's operational cost – USD 10 million for the 22 countries in scope for one molecule



*Cost sharing agreements between licensees and originators on other cost buckets such as regulatory may vary on a case by case basis. This analysis only takes into account cost that will necessarily be borne by the originator when doing VL

Voluntary licensing operational costs in USD million

Representativity: Large sample
Data source: Interviews with nine global access experts from six leading biopharmaceutical companies, IQVIA MIDAS
Geographies: UMICs & LMICs in which experts had experience
Cost categories: Consultancies and partnership management over 1 year

Methodology
1. Collect experts' estimation of bilateral licensing implementation costs for UMICs & LMICs
2. Multiply by the number of necessary processes to enter the 22 countries in scope (12 UMICs, 10 LMICs); assuming 7 countries can be entered at the same time based on experts' input
3. Compare with MPP costs (USD 0) to evaluate the avoided costs

A successful endeavour in voluntary licensing for vaccines: the mRNA Technology Transfer Programme

In 2021, WHO and MPP established a technology transfer Programme for mRNA vaccines, to build mRNA-based vaccines manufacturing capacity in low- and middle-income countries. The objectives of the Programme are to establish and enhance sustainable mRNA vaccine manufacturing capacity and to develop skilled human capital in regions with little or no current capability. The principal aim of the Programme is to strengthen health security by enhancing regional capacity to develop and manufacture mRNA vaccines, starting with vaccines for Covid-19; to create value and share IP through open access innovation, and promote sustainable capacity to produce mRNA vaccines with coherent policies and adequate investments. Fifteen manufacturing partners have been selected for the mRNA technology transfer Programme, each in a different LMIC. In just two years, the mRNA technology transfer Programme has made remarkable progress, producing a functional mRNA vaccine candidate product which is being evaluated in pre-clinical immunogenicity and efficacy studies and manufacturing partners from 13 countries have received hands-on introduction to the mRNA technology training from Afrigen. This will allow these manufacturing partners to develop, either singly or in partnership, new mRNA-based products but also to license in mRNA-based products developed by big pharmaceutical companies, providing the same benefits as highlighted in this report for therapeutics.

Dr. Drew Weissmann explains "RNA vaccines are going to change the way we manage many diseases, including beyond infectious diseases. Originators will not reach the right price point; they need GMP partners in low- and middle-income countries, and they need to consider voluntary licensing early to access all market segments. I think, in the next few years, we're going to see more and more of these GMP sites and research infrastructure sites across the world developing new and novel treatments. MPP, with its network and unique blend of skills is a critical accelerator[22]."

22. Penn Medicine news (2023). How Penn Medicine Is Changing the World with mRNA. Retrieved from : https://www.pennmedicine.org/news/news-blog/2023/november/how-penn-medicine-is-changing-the-world-with-mrna

PART 2 CONCLUSIONS

- **MPP's hands-on licence management model can reduce product diversion and ensure quality** through (i) trustworthy collaborations with partners; (ii) strict licensee selection processes; (iii) SRA approval requirements prior, and in addition to, the needed regulatory approval in each individual country; (iv) post-market surveillance mechanisms; (v) stringent trade dress requirements; and (vi) strong legal frameworks.
- **When product diversion is not mitigated, it can lead to yearly revenue loss for originators estimated to range between USD 2 million per LMIC and USD 8 million** per UMIC for sales of nine molecules.
- **Operational costs associated to licence management are estimated to reach USD 10 million to license one product in 22 countries.** These costs are completely avoided with MPP as a partner.

PART 3
-
THE BENEFITS OF VOLUNTARY LICENSING AS A HEALTH EQUITY STRATEGY

I. HEALTH EQUITY INCREASES TALENT RETENTION AND ATTRACTION, ESPECIALLY R&D TALENTS.

Despite the healthcare industry being purposeful by nature, only 62% of employees in this industry report engaging in meaningful work[23]. Employees increasingly expect their jobs to bring a significant sense of purpose to their lives and when asked about what would drive them to take a new job, employees' answers are focused among other factors on work they enjoy or care about[24]. Attracting and retaining employees are among the top motivators for organisations of all types to support workplace initiatives[25].

A former human resources director from a leading biopharmaceutical company reported that the sense of purpose has become non-negotiable for biopharmaceutical companies' talents[26] *"(…) we lost 25% of our candidates for lesser salaries because they wanted to go to a more mission-focused, purpose-driven company. There is a change in pharmaceutical companies' employee value proposition: it used to be about how much money you make, now it's about how you impact society"*. Strategies for talent retention and attraction should therefore be broad and focus on more than just salary.

Biopharmaceutical companies' human resources experts especially see a **shift in talents' expectations for global health equity strategies:** *"(…) global organisations are expected to have a global impact, notably through access strategies involving developing markets. Not showing that they care for individuals all over the world would be a huge deterrent for an organisation[26]"*.

Moreover, technical talent such as **R&D scientists in biopharmaceutical companies demonstrate their scientific interest in having access to a global patient base.** This is especially true for research in (i) clinical trials, (ii) advanced biology, (iii) infectious and emerging diseases[27]. Such talents are frequently head-hunted, and many biopharmaceutical companies are finding it challenging to recruit them. Today, very few biopharmaceutical companies are strongly positioned on R&D for therapeutic areas that concern primarily developing countries, and this positioning could be differentiating in technical talent attraction.

The ability to contribute to health equity and, more specifically, facilitate access to medicine with strategies such as voluntary licensing for instance, has increasingly become a priority for talents when applying for, and staying at, jobs at biopharmaceutical companies.

II. TALENT RETENTION CAN AVOID SIGNIFICANT HR COSTS IN RECRUITING AND TRAINING.

Analysis #8: Human resources costs reduction

Employee retention is understandably top-of-mind for many leaders and business executives. Interviews with five former human resources directors from four leading biopharmaceutical companies have helped estimate the impact of health equity strategies on human resources cost savings. They share that in high-income countries, biopharmaceutical companies' voluntary attrition rate of 10% per year, which is the industry average, could be reduced to 9% with strong global health equity strategies. **It has been estimated that this 1% difference represents a yearly cost reduction in recruitment and training ranging from USD 7 million to USD 50 million, depending on biopharmaceutical company size, training time and average salaries[28]. Since it is impossible to quantify, this does not take into account the critical competitive advantage that attracting and retaining the top talent can have.**

23. Great place to work (2022). Purpose offers opportunity for High Attrition Industries. Retrieved from: https://www.greatplacetowork.com/resources/blog/purpose-offers-opportunity-for-high-attrition-industries.
24. BCG (2023). More than a quarter of employees globally are ready to move on from their current jobs. Retrieved from: https://www.bcg.com/press/18december2023-employees-move-on-from-current-jobs.
25. BCG (2023). The future of work revolves around talent. Retrieved from: https://www.bcg.com/publications/2023/future-of-work-revolves-around-talent-management.
26. BCG interview with human resources director at leading biopharmaceutical company– October 2023
27. BCG interview with human resources director at leading biopharmaceutical company– October 2023.
28. BCG interviews with five former HR directors from four leading biopharmaceutical companies – October 2023.

ANALYSIS 8 - Human resources costs reduction

FIGURE 12 - Biopharmaceutical companies with strong health equity strategy can save up to USD 50 million in HR avoided cost

$ value estimation with average salary costs in $M per year of the impact on attrition rate around 1%

Representativity: Large sample
Data source: Interviews with five former HR directors from four leading biopharmaceutical companies
Scope: High-income countries in which experts had experience
Timeframe: 1 year
Cost categories: recruitment & 'up-to-speed' time (training & ramp-up)
Methodology
1. Collect experts' estimation of yearly costs in salary months of employee attrition and estimation of the impact of health equity on attrition rate depending on biopharmaceutical company size
2. Compute the reduction in attrition rate due to health equity efforts in salary months
3. Convert the salary month savings in dollar value by using the average salary of employees from three different levels of seniority (executives, managers, general employees) and their share among all companies' employees

III. THE IMPACT OF HEALTH EQUITY EFFORTS ON BIOPHARMACEUTICAL COMPANIES' COST OF BORROWING.

Biopharmaceutical's key lever for ESG impact lies in the social pillar and access to medicine is the key social factor for pharma companies. To measure this impact, accounting standards such as the Sustainability Accounting Standards Board (SASB) quantifies efforts towards ESG with tangible metrics. One of them is the access to medicines metric which refers to actions that promote access to healthcare products for priority diseases and in priority countries. This metric can be substantially influenced by voluntary licensing strategies as the Access to Medicines Index highly values voluntary licensing as a measure of access[29]. In this context, voluntary licensing is a means for biopharmaceutical companies to enhance their ESG performance on social criteria.

With the growing number of investments from environmental, social and governance (ESG) investors, issuance in the pharmaceutical sector will continue becoming increasingly popular. Sustainability-linked debt is an emerging area with strong growth potential for the pharma industry[30]. Sustainability-linked bonds (SLB), a subset of ESG bonds, are a type of instrument for which the financial or structural characteristics can vary depending on whether the issuer achieves predefined sustainability objectives, and, moreover, these bonds have reduced interest rates. Green, social, sustainable, and sustainability-linked bond issuance has risen in 2023, despite challenges posed by high global interest rates, while traditional bond issuance is stagnating[31].

COVID-19 has presented an opportunity for the pharma industry to demonstrate its importance to society. Biopharmaceutical companies' good ESG ratings can allow them to access SLBs which have proven to lower their borrowing costs while avoiding "social washing" as issuers have to achieve their KPIs to benefit from lower interest rates. Indeed, Novartis[32], Teva[33] and Sanofi[34] issued SLBs based on health equity objectives (e.g., larger access to essential medicines to treat NCDs in LMICs) and if the health equity objectives linked to the bonds were to be reached, **they could all save between USD 13 million and USD 34 million in annual borrowing costs[35] because interest rates linked to SLBs are lower than the companies' conventional borrowing interest rates.**

FIGURE 13 - : Biopharmaceutical companies leveraged SDG bonds with HE targets and saved up from USD 13 million to USD 34 million in borrowing costs per year

	NOVARTIS	teva	sanofi
Savings in borrowing costs per year	$ 34M	$ 33M	$ 13M
(=) total amount raised through SLBs	$ 2bn	$ 7.5bn	$ 0.7bn
(X) [conventional debt interest rate[1]	1.60%	6.60%	1.80%
(-) SLBs interest rate if objectives are reached]	0%	6.60%	1.25%
SLBs interest rate if objectives are not reached[2]	up to 0.75%	up to 7%	up to 2%

[1] Company interest rate taken into analysis is average of interest rates of bond issued with maturity & amount similar to SLBs maturity. [2] A penalty per year with objectives not reached is added

PART 3 CONCLUSIONS

- Health equity strategies such as voluntary licensing increase talent attraction and retention which can avoid significant costs in recruiting and training for biopharmaceutical companies. **These costs are estimated to range from USD 7 million to USD 50 million depending on company size, training time and average salaries.**
- Strategies such as voluntary licensing that improve access to healthcare products for priority diseases and in priority countries represent sustainability targets that allow biopharmaceutical companies to issue Sustainability-Linked Bonds. **These bonds have low interest rates and contribute to reducing biopharmaceutical companies' cost of borrowing.**

29. Access to Medicine Foundation (2022). 2022 Access to Medicine Index. Retrieved from: https://accesstomedicinefoundation.org/resource/2022-access-to-medicine-index
30. Unicredit (2020). European pharma: Sustainability-bond issuance. Retrieved from: https://www.research.unicredit.eu/DocsKey/credit_docs_9999_178624.ashx?EXT=pdf&KEY=n03ZZLYZf5miJJA2_uTR8ibqznDEa9efYLYGHlzWkEk=&T=1
31. S&P Global (2023). Global Sustainable Bonds 2023 Insuance Ti Exceed $900 Billion. Retrieved from: https://www.spglobal.com/esg/insights/featured/special-editorial/global-sustainable-bonds-2023-issuance-to-exceed-900-billion
32. Novartis. (2020). Final Listing Prospectus. Retrieved from https://www.novartis.com/sites/novartis_com/files/20200921-slb-final-listing-prospectus.pdf
33. Teva. (2023). Prospectus Supplement. Retrieved from https://s24.q4cdn.com/720828402/files/doc_downloads/2023/03/bannerless-final-prospectus-supplement_march-3-2023.pdf
34. Sanofi. (2022). SLB Prospectus. Retrieved from https://www.sanofi.com/dam/jcr:5c19adbd-767c-435d-8f46-ed5a9980bbcf/7y-Sustainability-Linked-Bond-Prospectus-April-2022.pdf
35. Company information, BCG analysis.

CONCLUSION

As demonstrated in this report, we believe that sharing IP through voluntary licensing can answer the strong global pressure for affordable access at scale, and can do so in a way that is transparent. It can also answer the equally strong pressure for more local production, especially in Africa.

The analyses in this report show that there are multiple financial benefits from engaging in voluntary licensing. While these benefits do not represent major commercial opportunities, when taken together they are not insignificant and, equally, with a partner such as MPP, they are very low risk.

Voluntary licences represent then much more than a humanitarian endeavour across all categories of products: not only do they enable originators to meet their access and ESG commitments and generate goodwill, but they also represent viable commercial strategies. Even for vaccines, voluntary licensing is the smart thing to do.

Jeremy Farrar, Chief Scientist at the World Health Organization: "We should make vaccines broadly available. it is enlightened self-interest: not only from a public health perspective but also for biopharmaceutical companies.[36]"

This argues for re reconsideration of voluntary licensing within biopharmaceutical companies. If they see it in more commercial and less CSR terms, in fact, more as an opportunity and less perhaps as some kind of 'obligation', then it will have more profile and priority within companies. This will mean more people understand it properly and the extraordinary flexibility it offers, while at the same time avoiding some of the drawbacks of other access approaches, such as lack of sustainability or risk of reference pricing.

This in turn would mean voluntary licensing becomes mainstream and is used far more than it is now. And that would make the dream of Universal Health Coverage attainable. We believe these benefits can even be **compounded as more and more biopharmaceuticals engage in voluntary licensing,** joining a movement that pushes forward equitable access to health, while also enhancing companies' global performance.

We should make vaccines broadly available. It is enlightened self-interest: not only from a public health perspective but also for biopharmaceutical companies."

Jeremy Farrar, Chief Scientist at WHO

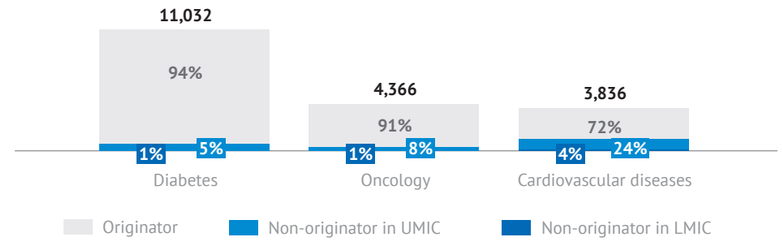
36. BMJ (2021). Jeremy Farrar, it's self-interest to share our vaccines globally. Retrieved from: https://doi.org/10.1136/bmj.n536

APPENDIX

This appendix is a detailed compendium of all the analyses underpinning the report. Each analysis contains the following information: (i) the level of representativity which informs the statistical power of the approach (essentially large sample versus case study); (ii) the data used (timeframe, source, geographical scope, molecules) and (iii) a step-by-step methodology to reproduce findings.

ANALYSIS 1 - Non-originator vs.originator sales

FIGURE 1 - Non-originators' sales constitute 6% to 28% of total sales per therapeutic area

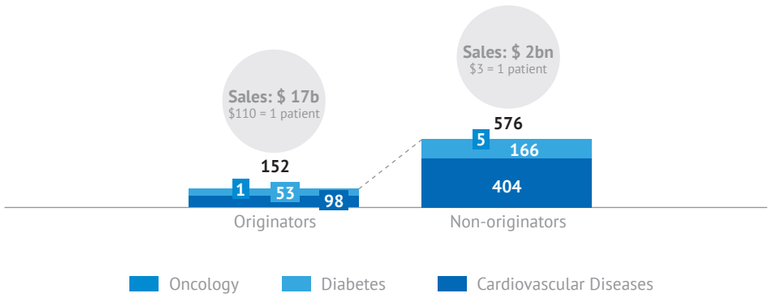


Average molecule sales in USD million, split between originators and non-originators

Representativity: Large sample
Data source: IQVIA MIDAS; extracted October 2023
Geographies: 22 countries
Timeframe: 2020 to 2022
TA: Diabetes; Oncology; Cardiovascular Diseases
Molecules: Atovarstatin; Bosentan; Fulvestrant; Glimepiride; Imatinib; Insulin Glargine; Metoprolol; Repaglinide; Trastuzumab (please see 'country data per molecule' in appendix for detail)
Methodology:
1. Identify originators vs. non-originators' products
2. Calculate sales for both per molecule and per country
3. Calculate the average for 2020, 2021, 2022

ANALYSIS 2 - Non-originator vs.originator patient reach

FIGURE 3 - Though non-originators represent only 11% of molecule sales; they reach x4 more patients



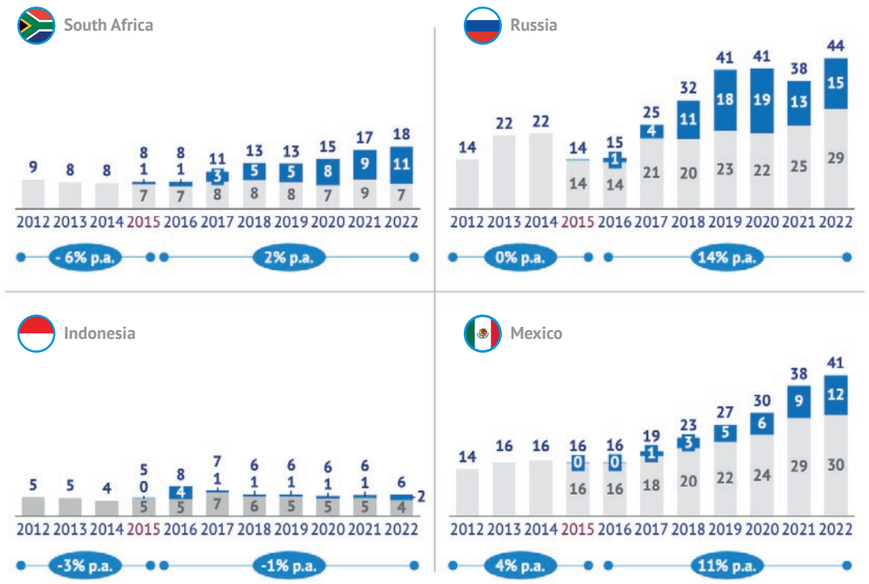
Yearly non-originators' patient reach in millions of patients

Representativity: Large sample
Data source: IQVIA MIDAS extracted October 2023; European Medicines Agency; Base de données publique des medicaments (FR); Vidal
Geographies: 22 countries (please see 'country data per molecule' for detail)
Timeframe: 2020 to 2022
TA: Diabetes; Oncology; Cardiovascular Diseases
Molecules: Atovarstatin; Bosentan; Fulvestrant; Glimepiride; Imatinib; Insulin Glargine; Metoprolol; Repaglinide; Trastuzumab

Methodology:
1. For each molecule, calculate a conservative yearly consumption of medicine boxes per patient
2. For non-originators and originators, divide the average number of sold boxes in each country with the yearly patient consumption
3. Compute the patient reach per therapeutic area for UMICs & LMICs & in total
4. Compare the difference between licensee's and originator's total

ANALYSIS 3 - Patient segments

FIGURE 5 - Metformin non-originators reached a new patient segment previously £ untapped by originator



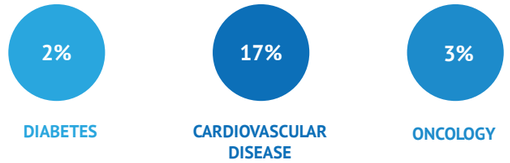
Metformin sales in USD million

Representativity: Case study
Data source: IQVIA data request; October 2023
Geographies: South Africa; Indonesia; Russia; Mexico
Timeframe: 2012 to 2022
TA: Diabetes
Molecules: Metformin

Methodology:
1. Identify a molecule where the originator is presentin a country; and new non-originators enter the market later on
2. Calculate the originator's compound annual growth rate (CAGR) before and after non-originator's entry

ANALYSIS 4 - Additional originator revenue

FIGURE 8 - Additional revenue from implementing royalties in UMICs could range 2% to 17% vs. originator sales

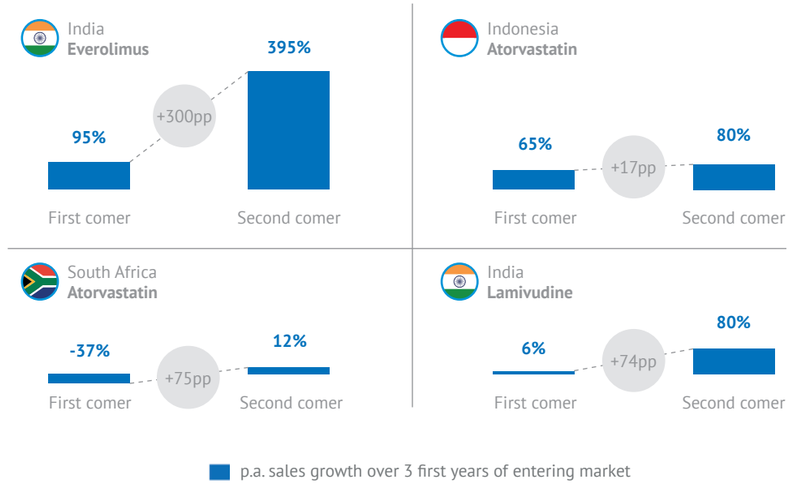


Estimated % of additional revenue for originators in UMICs

Representativity: Large sample
Data source: IQVIA MIDAS; extracted October 2023
Geographies: 22 countries
Timeframe: 2020 to 2022
TA: Diabetes; Oncology; Cardiovascular diseases
Molecule: Atovarstatin; Bosentan; Fulvestrant; Glimepiride; Imatinib; Insulin Glargine; Metoprolol; Repaglinide; Trastuzumab
Methodology:
1. Estimate cost of producing each molecule for non-originators in LMICs & UMICs; taking min. price point in India for GMP manufacturers with stable prices – conservatively assuming no margin
2. Calculate the average for 2020, 2021, 2022.
3. Multiply estimated cost of producing molecules per average volume of sales
4. Apply 60% revenue for originators on difference with cost; in UMICs & India only

ANALYSIS 5 - Market shaping

FIGURE 9 - Second comers' sales grew up to 4x more than first comers in their first 3 years



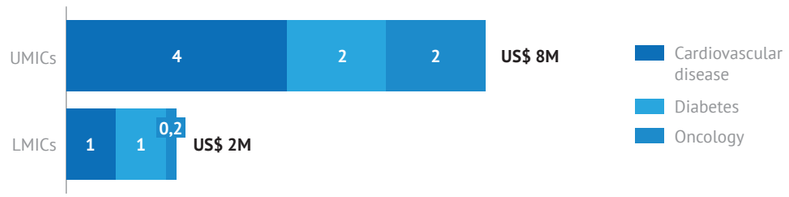
First comers & second comers' USD sales CAGR over first 3 years of entering market

Representativity: Multiple case studies
Data source: IQVIA data request; October 2023
Geographies: India; Indonesia; South Africa
Timeframe: 2012 to 2022
TA: Oncology; Cardiovascular Diseases; HIV
Molecule: Atorvastatin; Everolimus; Lamivudine

Methodology
1. Identify 2 different manufacturers for the same molecule in the same country, that entered the market at different times
2. Calculate CAGR for the 3 first years of the first to enter market; and the CAGR for the 3 first years of the second to enter market
3. Compare both

ANALYSIS 6 - Yearly revenue loss per country due to product diversion cost

FIGURE 10 - Yearly product diversion cost across therapeutic areas in USD million

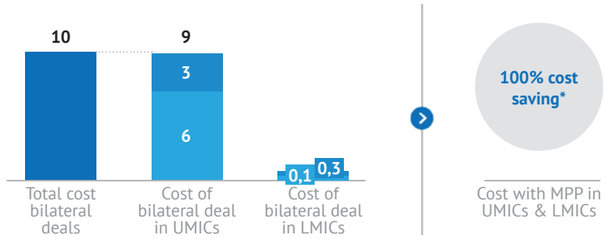


Representativity: Large sample
Data source: Interviews with nine global access experts from six leading biopharmaceutical companies, IQVIA MIDAS
Geographies: UMICs & LMICs in which experts had experience
Timeframe: 1 year
Product diversion: i) product stolen and sold illegally; ii) product copied to be sold illegally

Methodology
1. Collect experts' estimation of yearly product diversion costs in share of revenue
2. Assume that product diversion costs can be generalized to the scope of our study
3. Calculate the share of revenue loss due to product diversion, based on IQVIA average yearly revenue for each therapeutic area in scope of this analysis

ANALYSIS 7 - Annual operational costs

FIGURE 11 - By partnering with MPP, biopharmaceutical companies can avoid 100% of VL's operational cost –USD 10 million for the 22 countries in scope for one molecule



*Cost sharing agreements between licensees and originators on other cost buckets such as regulatory may vary on a case by case basis. This analysis only takes into account cost that will necessarily be borne by the originator when doing VL

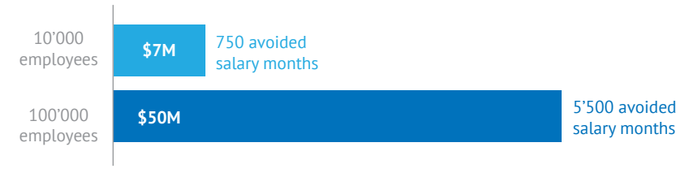
Voluntary licensing operational costs in USD million

Representativity: Large sample
Data source: Interviews with nine global access experts from six leading biopharmaceutical companies, IQVIA MIDAS
Geographies: UMICs & LMICs in which experts had experience
Cost categories: Consultancies and partnership management over 1 year

Methodology
1. Collect experts' estimation of bilateral licensing implementation costs for UMICs & LMICs
2. Multiply by the number of necessary processes to enter the 22 countries in scope (12 UMICs, 10 LMICs); assuming 7 countries can be entered at the same time based on experts' input
3. Compare with MPP costs (USD 0) to evaluate the avoided costs

ANALYSIS 8 - Human resources costs reduction

FIGURE 12 - Biopharmaceutical companies with strong health equity strategy can save up to USD 50 million in HR avoided cost



$ value estimation with average salary costs in $M per year of the impact on attrition rate around 1%

Representativity: Large sample
Data source: Interviews with five former HR directors from four leading biopharmaceutical companies
Scope: High-income countries in which experts had experience
Timeframe: 1 year
Cost categories: recruitment & 'up-to-speed' time (training & ramp-up)
Methodology
1. Collect experts' estimation of yearly costs in salary months
2. Compute the reduction in attrition rate due to health equity efforts in salary months
3. Convert the salary month savings in dollar value by using the average salary of employees from three different levels of seniority (executives, managers, general employees) and their share among all companies' employees

FIGURE 14 - Teva SLB's characteristics

Bond timeline	Sustainability-linked bond issue date	2021
	Date by which health equity objectives must be met	2025
	Bond maturity date	2029
Bond amount	Amount raised	$5 billion
Bond interests' characteristics	Interest rates before target date	4.5%
	Interest rates after target date if objectives are reached	4.5%
	Interes rates after target date if objectives are not reached	+0.45% per year

Bond timeline	Sustainability-linked bond issue date	2023
	Date by which health equity objectives must be met	2026
	Bond maturity date	2031
Bond amount	Amount raised	$2.5 billion
Bond interests' characteristics	Interest rates before target date	7.8%
	Interest rates after target date if objectives are reached	7.8%
	Interes rates after target date if objectives are not reached	+0.45% per year

FIGURE 15 - Sanofi SLB's characteristics

Bond timeline	Sustainability-linked bond issue date	2022
	Date by which health equity objectives must be met	2026
	Bond maturity date	2029
Bond amount	Amount raised	$721 million
Bond interests' characteristics	Interest rates before target date	1.25%
	Interest rates after target date if objectives are reached	1.25%
	Interes rates after target date if objectives are not reached	+0.25% per year

FIGURE 16 - Novartis SLB's characteristics

Bond timeline	Sustainability-linked bond issue date	2020
	Date by which health equity objectives must be met	2025
	Bond maturity date	2028
Bond amount	Amount raised	$2.1 billion
Bond interests' characteristics	Interest rates before target date	0%
	Interest rates after target date if objectives are reached	0%
	Interes rates after target date if objectives are not reached	+0.25% per year

FIGURE 17 - LMICs & UMICs data per molecule; IQVIA MIDAS Oct. 23

		Atorvastatin	Bosentan	Fulvestrant	Glimepiride	Imatinib	Insulin Glargine	Metoprolol	Repaglinide	Trastuzumab
UMICs	India	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Indonesia	✓	✗	✓	✓	✓	✓	✓	✓	✓
	Brazil	✓	✓	✓	✓	✓	✓	✓	✓	✓
	China	✓	✗	✓	✓	✓	✓	✓	✓	✓
	Mexico	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Russia	✓	✓	✓	✓	✓	✓	✓	✓	✓
	South Africa	✓	✗	✓	✓	✓	✓	✗	✗	✓
	Thailand	✓	✓	✓	✓	✓	✓	✓	✗	✓
	Argentina	✓	✓	✓	✓	✓	✓	✗	✓	✓
	Colombia	✓	✓	✗	✓	✓	✓	✓	✗	✓
	Malaysia	✓	✓	✓	✓	✓	✓	✓	✗	✗
	Turkey	✓	✓	✗	✓	✓	✓	✓	✗	✓
LMICs	Algeria	✓	✗	✗	✓	✗	✓	✓	✓	✗
	Bandladesh	✓	✓	✗	✓	✓	✓	✓	✓	✗
	Egypt	✓	✓	✓	✓	✓	✗	✓	✓	✓
	Jordan	✓	✓	✗	✓	✓	✗	✗	✗	✓
	Lebanon	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Morocco	✓	✗	✓	✓	✓	✓	✗	✓	✓
	Pakistan	✓	✓	✗	✓	✓	✓	✓	✓	✓
	Sri Lanka	✓	✓	✗	✓	✗	✓	✓	✓	✗
	Tunisia	✓	✓	✗	✓	✓	✓	✓	✓	✓
	Vietnam	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Total	**22/22**	**17/22**	**14/22**	**22/22**	**20/22**	**20/22**	**18/2**	**16/22**	**18/22**

FIGURE 18- Leading biopharmaceutical companies are shifting towards adding a Health Equity focus in their value statement / employer value proposition

Analysis of leading PharmaCos' value statement / EVP

	MERCK	Johnson&Johnson	BAYER	Pfizer	Roche	NOVARTIS
Global equity focus in 2012 - 2017 EVP	✗	✓	*Not available*	✗	✗	✗
Key words	*Delivering growth*	*Caring for the world, one person at a time*	-	*Leadership*	*Innovation*	*Reimagine medicine*
Global equity focus in 2012 - 2017 EVP	✓	✓	✓	✓	✗	✗
Key words		*Global diversity (...) developing global supply base*	*Health for all, hunger for none*	*Breakthroughs that change people lives*	*Integrity, courage, passion*	No change

✗ *No health equity focus* ✓ *Small health equity focus* ✓ *Strong health equity focus*

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