How to accelerate pharmaceutical R&D: A new framework for sharing IP with global health researchers.

21 February 2018

Clarke B. Cole, Researcher with the Access to Medicine Foundation

Katy Graef, Director with the BIO Ventures for Global Health (BVGH)

Summary

Pharmaceutical companies have deep expertise in the research and development (R&D) of new medicines and vaccines. In addition to conducting R&D in-house, they can accelerate R&D by sharing intellectual property (IP) assets with third-party researchers. This is a largely under-utilised approach, particularly for supporting the development of new and adapted products for people living in low- and middle-income countries (LMICs). In recent years, IP sharing for R&D has been pioneered mainly in the neglected disease space, for example by pharmaceutical companies opening up their compound libraries and data vaults to independent research groups. Importantly, IP-sharing agreements have the greatest potential public health benefit when they include terms for ensuring resulting innovations are rapidly made accessible to populations in LMICs.

For 10 years, the Access to Medicine Index has tracked how the world's largest pharmaceutical companies share IP assets to accelerate product R&D for high-burden and priority diseases. The 2016 Index found that 14 out of the 20 companies evaluated provided evidence of 32 instances in which they shared IP with research institutions or drug-discovery initiatives on terms that aim to support access to any resulting innovations in LMICs. Most of this IP sharing aimed to accelerate R&D for HIV/AIDS, lower respiratory infections, malaria, tuberculosis and neglected tropical diseases.

In collaboration with BIO Ventures for Global Health, the Access to Medicine Foundation has now developed a new framework for evaluating industry IP-sharing agreements for R&D. The framework will be used for the first time as part of the 2018 Access to Medicine Index analysis. The framework compares different IP-sharing agreements in terms of risk, effort and potential value to accelerating R&D. This paper describes the framework, how it was developed and how it can be used by pharmaceutical companies to guide the development of IP-sharing strategies to accelerate R&D for global health needs.

Introduction

Pharmaceutical research and development (R&D) is an important means to improve health outcomes for populations in low- and middle-income countries (LMICs), where needed treatments, methods of prevention and cures do not exist or are inadequate. Often, needed pharmaceuticals are unavailable because they target diseases that predominantly affect the poorest populations globally, and therefore commercial market incentives are too low to drive necessary R&D. Pharmaceutical companies can support R&D for such high-burden and priority diseases through both in-house and collaborative R&D. Further, they can help to accelerate R&D by sharing intellectual property (IP) assets (e.g., unpublished data, compound libraries, compound sets) with third-party researchers who are working to develop new and adapted products that address the needs of LMIC populations. Importantly, various types of IP assets – even those that may not seem valuable to a company – can help accelerate the R&D activities of global health researchers.

Since 2008, the Access to Medicine Index has been analysing 20 of the largest R&D-based pharmaceutical companies by revenue on how they address access to medicine in LMICs. One metric used in this analysis (E.III.2 – IP sharing) assesses whether companies share their IP with research institutions that develop products for high-burden and priority diseases on terms that support access to resulting innovations in LMICs.

The 2016 Index found that 14 out of the 20 companies evaluated provided evidence of 32 instances of such IP sharing. Most of these instances aimed to accelerate R&D for HIV/AIDS, lower respiratory infections, malaria, tuberculosis and neglected tropical diseases (NTDs). AbbVie, Eisai, GSK, Merck KGaA, and Takeda engaged in the most IP sharing among companies measured by the Index, when taking company size into account.

In 2017, as part of the methodology review of the Access to Medicine Index, the Access to Medicine Foundation and BIO Ventures for Global Health (BVGH) undertook a review of this key measurement of the Index, combining their expertise in measuring and stimulating R&D according to global health needs. As part of this review, a new framework was developed that allows for a deepened analysis of companies' activities in this area. This new framework will be used to evaluate companies in the 2018 Access to Medicine Index. It will continue to recognise companies for engaging in IP-sharing agreements that support R&D that addresses the needs of populations in LMICs, and it will newly compare different IP-sharing agreements in terms of risk, effort and potential value to accelerating R&D. The framework can be used by pharmaceutical companies to guide their identification and engagement in IP sharing that is of greatest value to pharmaceutical R&D for high-burden and priority diseases.

Case studies: pharmaceutical companies that share IP to accelerate R&D

The following collaborations have been established through the WIPO Re:Search consortium – a programme managed by BVGH and the World Intellectual Property Organization. The Consortium aims to accelerate product development for malaria, tuberculosis, and NTDs. Through the Consortium, BVGH has established more than 120 research collaborations involving the sharing of IP assets, including 25 established since 2016. Of these collaborations, 17 include one of the eight pharmaceutical companies that are members of the Consortium and also evaluated in the Access to Medicine Index: Eisai; GSK; Johnson & Johnson; Merck KGaA; Merck & Co., Inc.; Novartis; Pfizer; and Takeda. These companies have agreed to include terms that promote access to resulting products in Least Developed Countries in research partnerships that arise out of WIPO Re:Search.

Case 1

Company: Merck & Co., Inc.
IP asset: HMG-CoA reductase inhibitors (statins)
Recipient: University of California, San Francisco (UCSF)
Potential innovation: new schistosomiasis treatment

In 2012, Merck & Co., Inc. shared a set of HMG-CoA reductase inhibitors – also known as statins, which were originally developed to treat high cholesterol – with a schistosomiasis researcher at UCSF. The UCSF researcher tested these inhibitors against the parasitic worm that causes schistosomiasis – *Schistosoma mansoni* – to determine whether these compounds could be promising schistosomiasis drug leads.

Case 2

Company: Pfizer
IP asset: modipafant data
Recipient: 60 Degrees Pharmaceuticals (60P)
Potential innovation: new dengue treatment

Pfizer disclosed data in 2013 – including its Investigator's Brochure, which includes details of an entire development programme – for its discontinued drug modipafant with 60P, a company that specialises in drug development for tropical diseases. Originally under development by Pfizer to treat asthma, modipafant is seen by 60P as a potential treatment for dengue fever. Using pre-clinical, clinical and chemistry, manufacturing and controls data supplied by Pfizer, 60P was able to save time and money and expedite modipafant's entry into clinical trials for dengue. If 60P's clinical studies achieve their clinical endpoints, the company estimates that modipafant will be approved to treat dengue fever by 2022.

Identifying IP sharing with high potential for accelerating R&D

IP sharing to accelerate R&D requires, in addition to a willing third-party researcher, alignment between a pharmaceutical company's R&D and IP divisions. Its R&D division develops the IP and thus has a deep understanding of its potential for broader use, whereas its IP division understands the company's overall approach to IP management, including its willingness to share IP and on what terms it will do so. Aligning these parts of the business requires strong communication and collaboration.

It is important to acknowledge that depending on the assets, companies assume varying degrees of risk, cost and effort when sharing IP. This can make IP-sharing arrangements more or less attractive to a company. Further, the value of the assets to the recipient can vary, depending on factors such as the degree to which the asset is likely to accelerate the recipient's product candidate to market. Importantly, the value of an IP asset to a company is not necessarily the same as its value to a third-party researcher. Companies need incentives to share IP with the greatest potential to support R&D that addresses the needs of populations in LMICs, and these incentives need to take into account the varying effort and risk required to do so.

To ensure innovations that arise from IP sharing have the greatest impact on global health, companies should further aim to base their IP-sharing agreements on terms that are conducive to ensuring rapid access to resulting innovations in LMICs upon approval.

How the new framework was developed

The Access to Medicine Foundation worked with BVGH, which drew on its expertise developed through co-management of the WIPO Re:Search consortium, to develop a framework for assessing the varying effort, risk and benefit of different IP-sharing agreements. The Foundation will use this framework to compare new IP-sharing agreements of the 20 pharmaceutical companies evaluated in the 2018 Access to Medicine Index. The Index analysis will publicly recognise, in its scoring system, companies that make the greatest efforts and take on the greatest risks to share IP with the greatest potential to accelerate R&D according to the needs of populations in LMICs. The results will be published in November as part of the 2018 Index report.

The new framework can also be used by pharmaceutical companies to improve their approaches to IP sharing, from identifying assets with the greatest potential to accelerate R&D for global health, to sharing those assets with external researchers through access-oriented IP sharing agreement.

Methodology

To develop the updated framework, all IP assets that pharmaceutical companies have shared with academic, non-profit, and government scientists through WIPO Re:Search between 2012 and 2017 were reviewed and then categorised. The result was a list of 11 asset types (see Table 1), all of which are valuable to R&D for high-burden and priority diseases. The asset types differ on factors including phase of development and publication status. Each asset type was rated on a set of six criteria.

Six criteria for rating IP-sharing agreements

Regarding the company sharing the IP:

1. Asset value: Measure of the relative monetary value (if any) a company would place on its asset.
2. Risk: How much risk to a company's business investments, pipeline and interests a company would assume by sharing the asset.
3. Effort: How much cost and effort a company would invest in preparing the asset for sharing. This includes time and costs associated with, for example, developing material transfer agreements, preparing compound libraries, dispensing and shipping libraries and identifying and redacting data.

Regarding the researcher receiving the IP:

4. Asset value: Measure of the relative value (both monetary and non-monetary) of the asset to a researcher.
5. Benefit: How much a researcher would benefit from using the asset. More specifically, the relative reward of applying the IP asset to a research project (i.e., probability of the research resulting in a product for a high-burden or priority disease) versus the risk a researcher assumes by using the asset (i.e., the amount of resources [in time] necessary to assess the asset).
6. Acceleration to market: A measure of how much of a leap of acceleration access to the asset would provide to a researcher's product development project for a high-burden or priority disease.

Next, three Associate Directors within BVGH individually applied a five-point scale to rate the relevance of the six criteria to each type of IP asset. The BVGH staff members based these five-point ratings on (1) their experience establishing R&D collaborations within WIPO Re:Search, (2) their knowledge of academic and non-profit researchers' projects, infrastructure and needs, and (3) their knowledge of the pharmaceutical company assets that can best meet those needs and accelerate R&D. A consensus-building process among the raters was subsequently employed to determine a single rating per criterion for each asset type. Next, a researcher at the Access to Medicine Foundation aggregated the findings to facilitate their application to the Access to Medicine Index indicator E.III.2. This involved classifying the asset types into three bands that reflect the overall (1) value of the asset to the company, and risk and effort taken by the company to share the IP and (2) value and benefit of the asset to the researcher and potential to accelerate the researcher's product candidate to market.

The methodology and findings were reviewed by senior experts from BVGH and the Access to Medicine Foundation. Further validation of this rating system by external experts will help to deepen its robustness for future use, both by relevant stakeholders and in future iterations of the Access to Medicine Index. Specifically, feedback provided during the 2019 methodology review can influence the use of this metric in the 2020 Access to Medicine Index. The results of the exercise are presented in Table 1 on the following page.

Table 1. Which IP assets have the greatest potential?

The 2018 Index will use this framework to recognise companies that share their IP with research institutions that develop products for high-burden and priority diseases on terms that support access to resulting innovations in LMICs. The framework assesses 11 types of IP assets, all of which are valuable to product R&D for high-burden and priority diseases. Each asset type is rated on a five-point scale according to its relevance to each criterion (one being the least relevant and five being the most). N/A indicates the criterion not applicable to the particular asset type. The ratings are aggregated to determine an average weight per asset type. This weight is used to place the asset type into one of three bands: assets in the 'greatest' category, for example, include those that pose a greater risk or effort to the company, but also have the greatest value to R&D that addresses global health needs. Companies can use this framework to guide IP-sharing strategies.

	Criteria							
	Company			Researcher				
Asset type	1 Asset value to company	2 Risk to company	3 Effort for company	4 Asset value to researcher	5 Benefit to researcher	6 Acceler-ation to market	Average weight	Band
Large diverse compound library - structures blinded	1	1	5	2	1	1	1.8	Least
Unpublished data - discovery stage	N/A	1	3	5	5	1	3	Moderate
Target-specific compound sets - discovery-stage	3	3	5	4	3	1	3.2	
Target-specific compound sets - pre-clinical-stage, deprioritised/no longer active in pipeline	3	1	5	4	3	3	3.2	
Proprietary or miscellaneous reagents	N/A	1	3	5	5	N/A	3.5	
Target-specific compound sets - clinical-stage, deprioritised/no longer active in pipeline	3	1	5	5	3	4	3.5	
Unpublished data - pre-clinical	N/A	1	5	5	5	3	3.8	Greatest
Performing assays for collaborator (e.g. mechanism of action studies)	N/A	1	5	5	5	N/A	4	
Unpublished documentation (e.g. synthesis methods)	5	5	3	2	5	N/A	4	
Target-specific compound sets - pre-clinical-stage, prioritised/active in pipeline	5	5	5	4	3	3	4.2	
Unpublished data - clinical-stage	N/A	1	5	5	5	5	4.2	

How the 2018 Index will measure IP sharing

The 2018 Index will apply this framework to deepen its analysis of company engagement in IP sharing. As for previous Indexes, the IP-sharing metric will give credit to companies for making agreements to share IP with research institutions that develop products for high-burden and priority diseases on terms that support access to resulting innovations in LMICs. Each IP-sharing agreement a company enters into between 2016 and 2018 that meets these inclusion criteria will be classified and weighted using the new framework. The company will be assigned a score based on the overall weight of the IP-sharing agreements they have entered into, relative to the performances of other companies evaluated. The results of this analysis will recognise the different risks and efforts companies take when sharing IP, along with the different values of this IP to supporting R&D for global health needs.

It is important to recognise that all IP sharing agreements that meet the described inclusion criteria are valuable in supporting R&D for high-burden and priority diseases. For example, large diverse compound libraries are an important means for external researchers to identify new avenues for research that may not have been previously considered. Thus, while they may be less valuable than other IP assets in the framework to support the development of specific product candidates, they are still important for global health R&D.

How companies can use the framework

Pharmaceutical companies can use the framework to develop their IP-sharing approaches, identifying and engaging in more opportunities to accelerate R&D for global health by sharing their IP with third-party researchers. Companies can increase their efforts to identify assets that have potential to benefit external R&D that addresses global health needs, where the company does not have plans to pursue such R&D internally. While each individual asset will vary in nature, the framework can be used as a guide for companies to understand how they may be impacted when sharing a particular asset type: in terms of the efforts and costs associated with sharing it, and the value of the asset to the company. Companies can use this information to better understand their capacity to share different IP assets.

Importantly, the framework can also be used to gauge the potential benefit of the asset to meeting global health needs, should it be applied to further R&D. First, companies can refer to the disease scope of the Index to identify diseases for which barriers to access are high in LMICs. This includes a list of diseases for which further R&D is a particularly high global health priority. Further, the framework can be used by companies to better understand the ability of different asset types to benefit the research of recipients, and to enable companies to prioritise sharing of assets that are most likely to benefit the recipient and accelerate R&D.

Collaboration with organisations such as BVGH can play an important role in supporting companies in this process – from understanding R&D priorities to identifying potential partners and supporting the development of IP-sharing agreements that promote access to resulting innovations in LMICs.

About the authors

Clarke B. Cole is a Researcher at the Access to Medicine Foundation, responsible for analysis of companies' activities in supply, registration, pricing, licensing and donations for the Access to Medicine Index. With a background in global health policy, she has conducted global health research for organisations including LSE Health, University of Ottawa and University of Toronto.

Katy Graef is a Director at BIO Ventures for Global Health who works across BVGH's programmes focused on expanding access to cancer medicines and technologies in Africa, accelerating R&D for diseases of poverty and building biomedical R&D capacity in low- and middle-income countries. With a background in infectious diseases, she has conducted biomedical research at the University of Washington, University of Oxford, and the National Institutes of Health (NIH).

About the Access to Medicine Foundation

The Access to Medicine Foundation is an independent non-profit organisation based in the Netherlands. It aims to advance access to medicine in low-and middle-income countries by stimulating and guiding the pharmaceutical industry to play a greater role in improving access.

About BIO Ventures for Global Health

BIO Ventures for Global Health (BVGH) is a non-profit organization working at the crossroads of the private and public sectors to advance research and improve health. BVGH connects people,

resources, and ideas across biotechnology and pharmaceutical companies, governments, and non-profits to solve global health issues.