Public Health & Economic Impact Study of NIH Intramural Technology Transfer Licensing: Final Project Report

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RTI INTERNATIONAL

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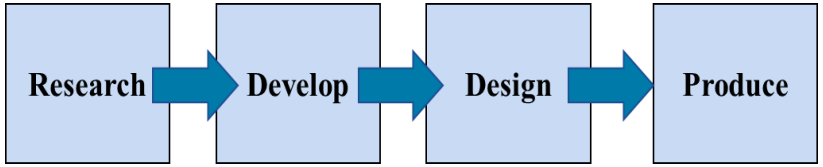
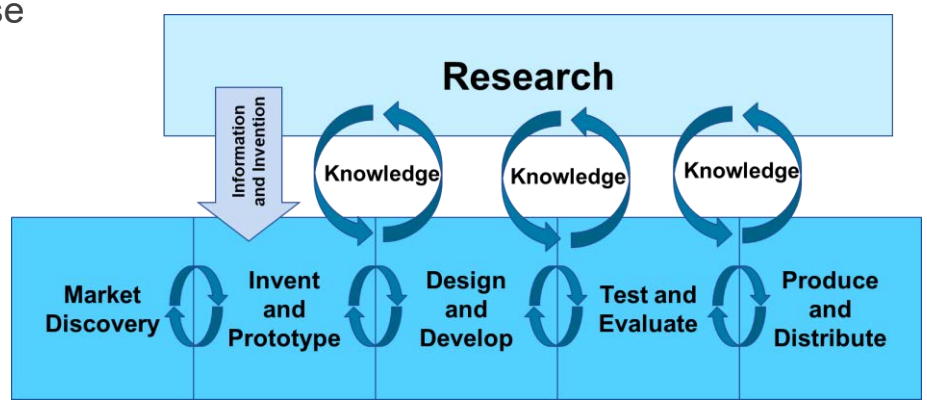


The technology transfer offices of the National Institutes of Health (NIH) are charged with facilitating the use of inventions generated by the NIH Intramural Research Program (IRP) in the development of new biomedical innovations that benefit the United States. The NIH, in accordance with its mission, conducts fundamental research to advance biomedical science that can lead to new therapies, vaccines, diagnostics, and other medical products. The private sector has responsibility for the development and sale of biomedical products and solutions that are launched on the market and improve the health of the U.S. population, and potentially the world. Under the Federal Technology Transfer Act of 1980 and its amendments, NIH technology transfer offices (TTOs) are critical actors in the diffusion and commercialization of the discoveries and inventions of NIH-employed researchers, leading to improvements in US biomedical innovation, US economic prosperity, and public health.

This report provides a portfolio of indicators that help to characterize and quantify the impact of IRP research enabled by technology transfer. A common but simplistic view of federal government research is that any discoveries flow automatically on a linear path into applied research and technology development, leading to new products and services (see Figure 1). The actual path from fundamental discovery to applications and products is much more complex, where research continuously informs product innovation and vice versa (see Figure 2). As a government agency, the NIH does not produce or sell commercial products, and so it relies on the private sector to use its biomedical discoveries and inventions as the basis of innovative therapies, treatments, instruments, and other technologies. The NIH's TTOs negotiate the licenses under which those commercial partners compensate NIH for the use of its inventions through royalty payments.

Figure 2: The Chain-Linked Model of Innovation



Beyond this financial remuneration, the TTOs play a critical role in ensuring that discoveries and inventions generated by IRP researchers contribute to innovations, products, and other tangible outputs that enhance the nation's ability to prevent, treat, and possibly cure the full range of diseases, syndromes, and conditions affecting the population of the US and of the world. The processes for protecting NIH intellectual property, identifying commercialization partners, negotiating agreements, and even arranging possible ongoing collaborative research are all under the purview of the TTOs, and all contribute to ensuring that the nation receives the maximum benefit possible from investments in the IRP.

Impact Pathways for IRP-Generated Inventions

This report presents a portfolio of quantitative and qualitative indicators that attempt to characterize the nature and scale of the impact that NIH-licensed inventions have in three domains:

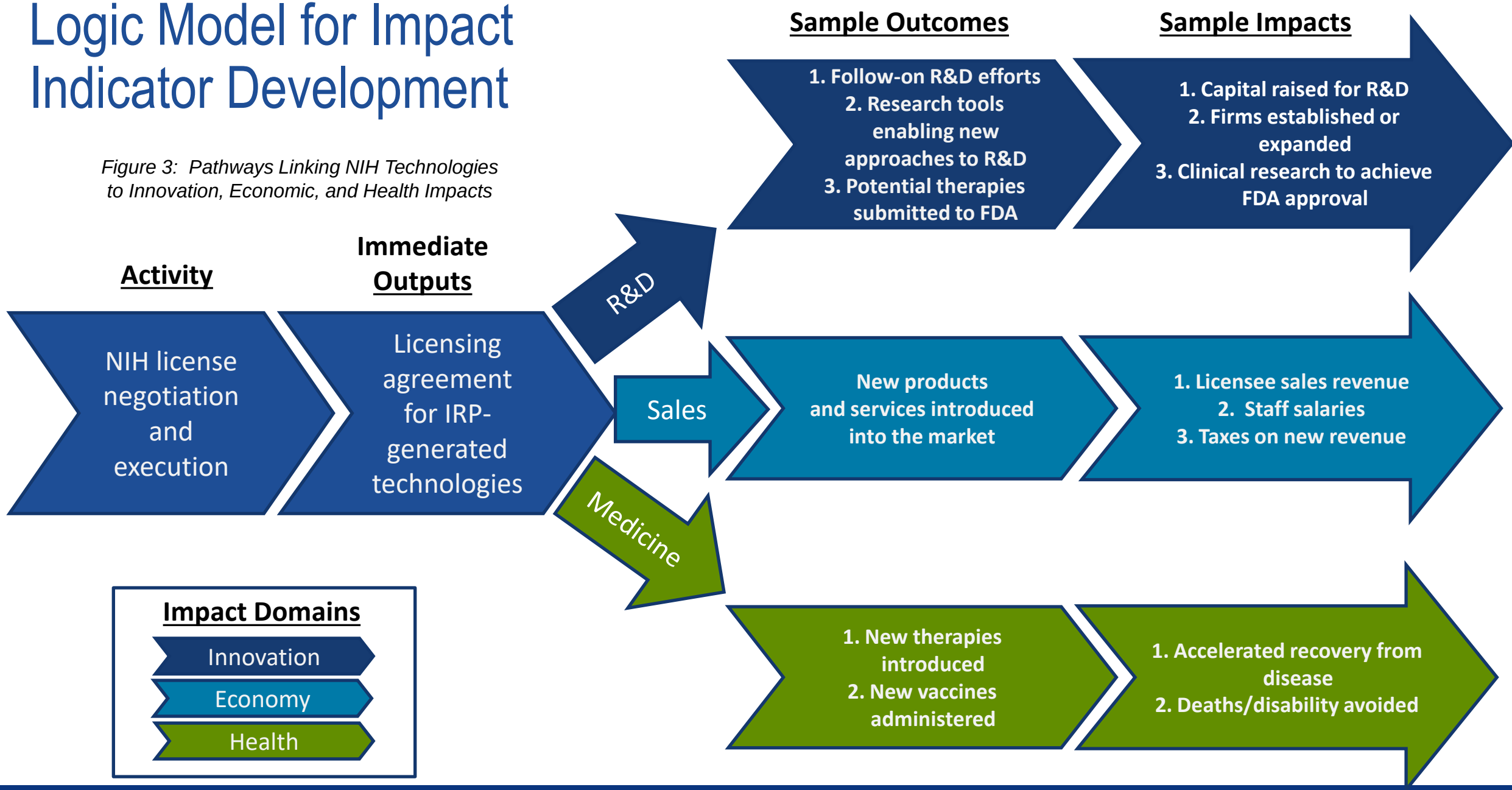
- Impacts on the biomedical innovation ecosystem, illustrating the role that NIH IRP licensing has played as a source of new technologies brought to market by early-stage companies, in spurring follow-on invention, in improving research capabilities through IRP-generated research tools, and in spurring new partnerships to conduct follow-on R&D and clinical trials.
- Impacts on the U.S. economy, showing how products based on these inventions lead to new revenues for licensees, employment growth, and contributions to Gross Domestic Product (GDP). For some technologies, the commercialization process can take several years. For example, candidates for therapeutic drugs will undergo further pre-clinical development and testing, and then enter the approval process required by the Food and Drug Administration (FDA), entailing multiple phases of clinical trials to meet regulatory standards. In such cases, the economic impacts may take as long as a decade to emerge.
- Impacts on the health of the U.S. and global public, as seen through measures such as the reduction in disease burden. Evidence of these impacts tend to emerge long after an invention is licensed. In these cases, the technology must first be commercialized as a treatment for a disease or condition, and then must be adopted by healthcare providers and administered to a significant patient population before significant impacts can be tracked. Exceptions to this pattern exist; for example, the rapid commercialization of the vaccines to immunize the world population against COVID-19 produced an impact on human health within a few years.

The diagram on the next page illustrates the pathways by which inventions generate these types of impact. As a general pattern, each pathway begins when the NIH identifies a potential commercial partner interested in the invention. Once a licensing agreement is reached, that partner will conduct substantial follow-on research and development, release a product for sale, and distribute the resulting medications, treatments, or devices.

For each pathway, we can see how the near-term outcomes of a pathway lead to longer-term impacts. For example, an early-stage firm that licenses an invention from the NIH will need to conduct research and development to create a potential new drug that can be submitted to the FDA for approval. That firm will then need to raise capital for clinical trials (inducing new investment in R&D activities), expand operations as it moves to production, and then work with research partners to help it bring the drug to market. That firm may end up being acquired by a large pharmaceutical firm with the resources to support later-stage clinical trials, scale up manufacturing, and market the drug through its existing distribution channels.

Logic Model for Impact Indicator Development

Figure 3: Pathways Linking NIH Technologies to Innovation, Economic, and Health Impacts



The Indicator Development Process

Technology transfers from the NIH intramural labs to external parties can vary substantially in many respects, including the type of invention involved, the market sector of the licensee, the scope of the license, and the significance of the patented technology to the resulting product or process. Those variations, in turn, lead to a diversity in the mechanisms and forms by which these transactions generate impacts on the US and the world. No single statistic or metric can capture the breadth and scale of benefits that NIH-licensed technologies may generate addressing national needs, such as economic prosperity, technological competitiveness, and public welfare.

By producing a suite of indicators (as defined in the text box on this page), this project attempted to capture the multiple facets of the "impact" of NIH-licensed inventions, addressing the potentially disparate views of the IRP's stakeholders. The indicators included in this report were selected based on multiple criteria:

- The indicators are orthogonal, in that each indicator represents a unique aspect of one of the three different domains of impact.
- The indicators are systematic, with each indicator generated through a particular process of data collection and analysis so that it can be replicated by others in the future and will produce consistent measurements over time.
- The indicators are representative of impact, meaning that the explanation of the relationship between the indicator and the type of impact represented is based on a transparent and defensible rationale.

These indicators are also designed to be practical. Each indicator uses data that can be obtained within reasonable effort, so that they can be updated regularly into the future without a significant investment of resources.

Defining Indicators

An indicator is "a quantitative (or qualitative) representation that might reasonably be thought to provide summary information" about a particular phenomenon or entity.[1]

Well-known economic and social indicators include Gross Domestic Product (indicating the scale of a national economy) and life expectancy (indicating overall population health). These indicators are not necessarily precise, but they provide a systematic and transparent method of generating comparisons of economic output and physical well-being.[2]

For this project, impact indicators take a variety of forms, including statistical charts and tables, graphical representations of relationships, and narrative case studies illustrating specific instances of impact.

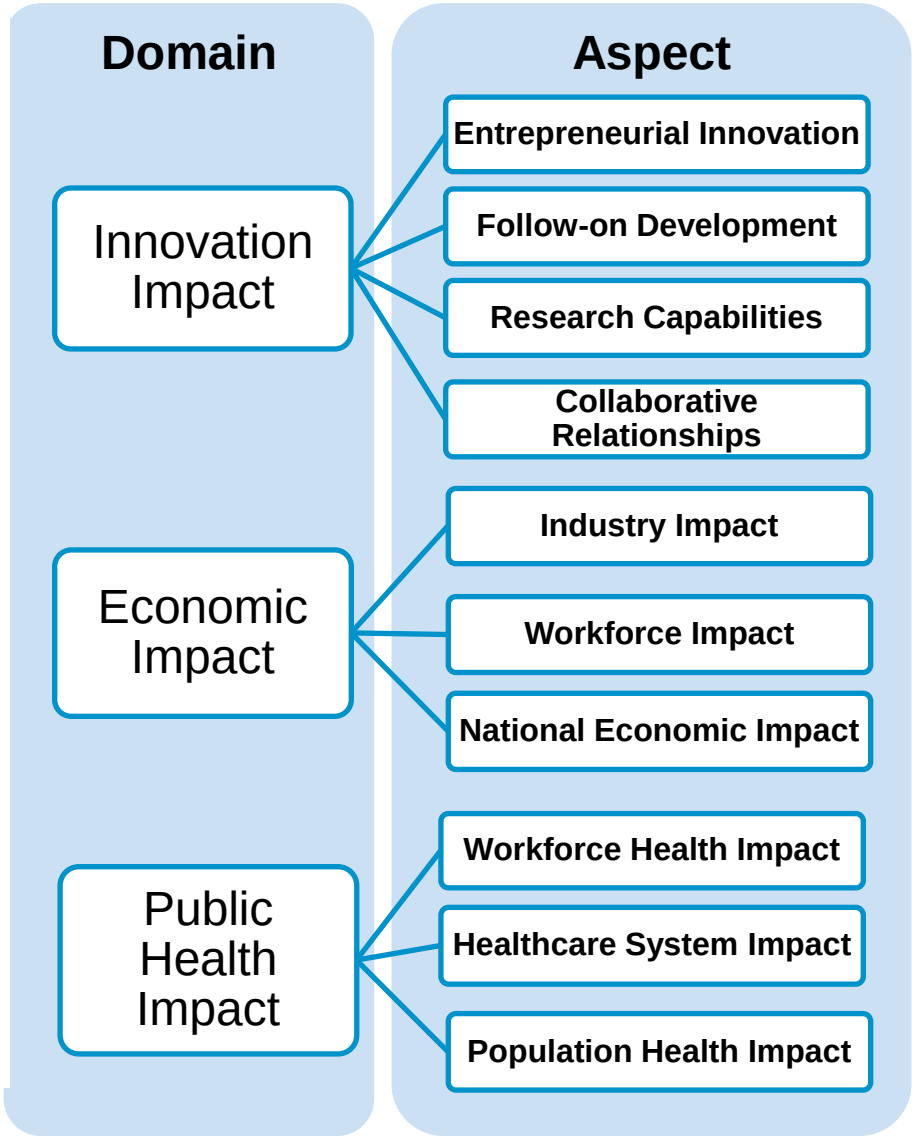
Developing Indicators by Aspect of Impact

To ensure that the portfolio of indicators captures a comprehensive range of impacts from the licensing of IRP-generated inventions, each of the three domains (innovation, economic, and health impacts) is further decomposed into multiple "aspects." Each aspect characterizes a certain set of desired effects of NIH technology transfer within a given domain. The aspects provide a way to connect specific activities or outcomes measured by the indicators to the broader domain of impact.

For example, previous studies illustrate the economic benefits of federal technology transfer. Technologies commercialized by private firms based on laboratory innovations and discoveries lead to the development or improvement of products introduced to the market, which in turn leads to increased sales by firms operating in the U.S.; additional employment at those firms, their suppliers, and their customers; and overall improvements in the productivity and output of the U.S. economy. To capture these various aspects of economic impact, indicators presented in this report show the estimates of new revenue for firms generated by products using NIH-licensed technologies. Using an analytical technique called input-output (I-O) modeling, the indicators estimate how those additional revenues translated into employment impacts, increases in the national tax base, and overall gains in Gross Domestic Product.[3]

Note that this approach (and the approach used for other indicators) does not allow us to calibrate our results based on the relative contribution of the NIH technology to the final product. In some cases, the NIH-licensed invention was the core technology that was essential to the development of the product (see the Case Study Appendix for examples). In other cases, the NIH contributed one among many enabling technologies involved in a new product. The indicators, in general, attribute the full impact of a product to the NIH-licensed technology, as estimating the marginal impact would require detailed analysis of every product, including licenses where the NIH may not know the exact product.

Figure 4: Identified Aspects of Impact Across Domains



The Indicator Development Process: Linked Data Approach

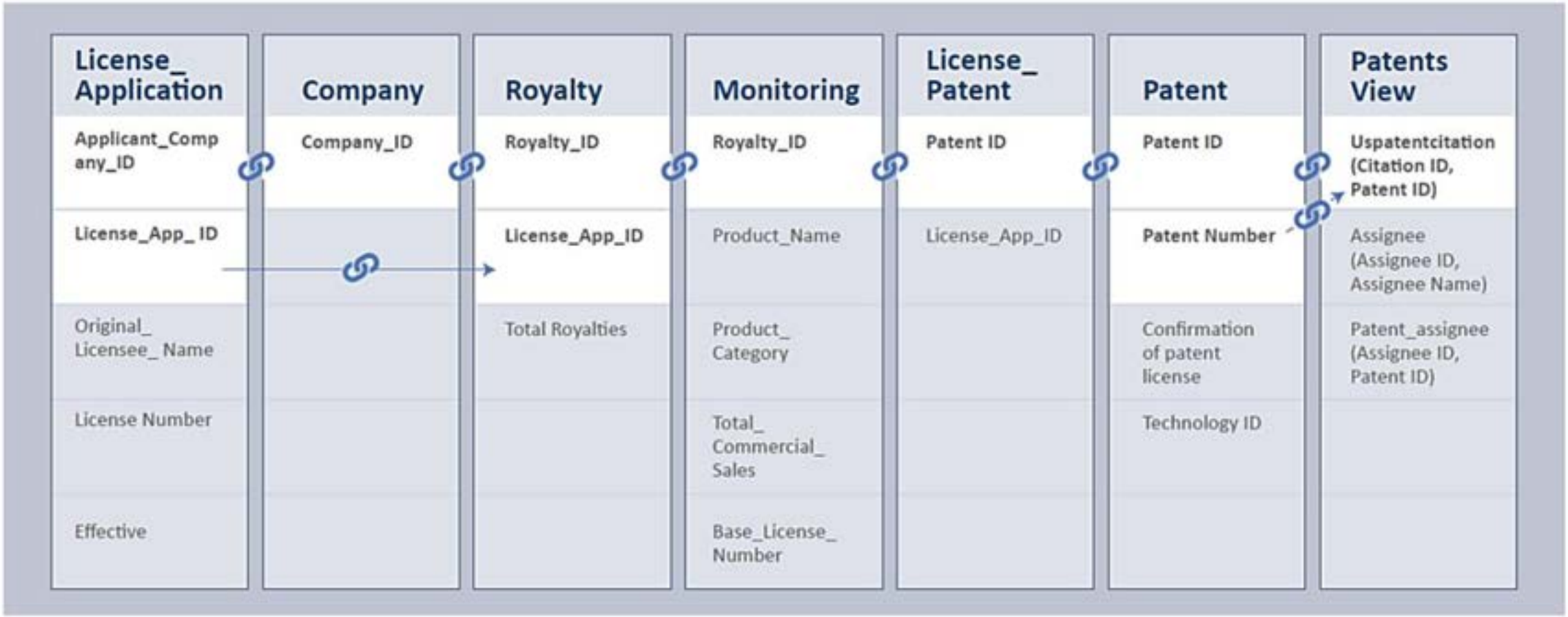
As part of the preparation for this project, the NIH Office of Technology Transfer provided the RTI team with access to the tables of data that form the infrastructure for the NIH TechTracS system. This system stores information about NIH patents, inventions, license applications, license agreements, and related details in a structured database. RTI generated its own data dictionary to describe the variables (fields) contained in each table and what each field represents. RTI then reassembled the tables to generate a new set of tables showing the attributes of each licensing agreement executed by NIH, containing information such as the license agreement number, the date of execution, the name of the licensee, the products developed using those licensed inventions, etc.

To generate indicators of impact, we need to related licensing agreements to the immediate outputs (products) and then to external data sources that measure impact in the individual domains. For example, one of our indicators of impact on the biomedical innovation ecosystem traces how an NIH-licensed invention contributes to later technology development by identifying all of the licensee's patents that cite the licensed NIH patent. (A patent citation signifies recognition that the citing patent somehow related to the invention protected by the cited patent.) To do this, we needed to look at each license, identify the specific NIH patents that were licensed to the licensee, and then use an external database called PatentsView[4] that provides the citation links between patents issued by the U.S. Patent and Trademark Office (see Figure 5, next page). The data linking process to generate an indicator involves establishing relationships between unique identifiers found across data tables and sources. In this example, the TechTracS table cataloging license applications has two key fields: an identification number for the applicant company and a number for the license application.

- With the Company ID, we can use the Company table to retrieve the applicant's name.
- By linking the License Application ID to the Royalty table, we can establish that the application led to a licensing agreement (represented by the Royalty ID), and the total royalties generated by the license.
- The Royalty ID is also found in the Monitoring table, which provides additional information such as the name of the product commercialized using the licensed technology, the sales generated by the product, and the formal licensing agreement number.
- The License_Patent table provides the identifiers for the NIH patents associated with the License Application ID for that agreement.
- The Patent table contains the actual US Patent Number associated with each Patent ID.
- The US Patent Numbers can be located in PatentsView to retrieve information on any citing patents granted to the licensee firm.

The Indicator Development Process: Linked Data Approach
Example from Indicator for Follow-on Technology Development

Figure 5: Data Linking Process to Associate Licensed NIH Inventions to Follow-on Technology Development

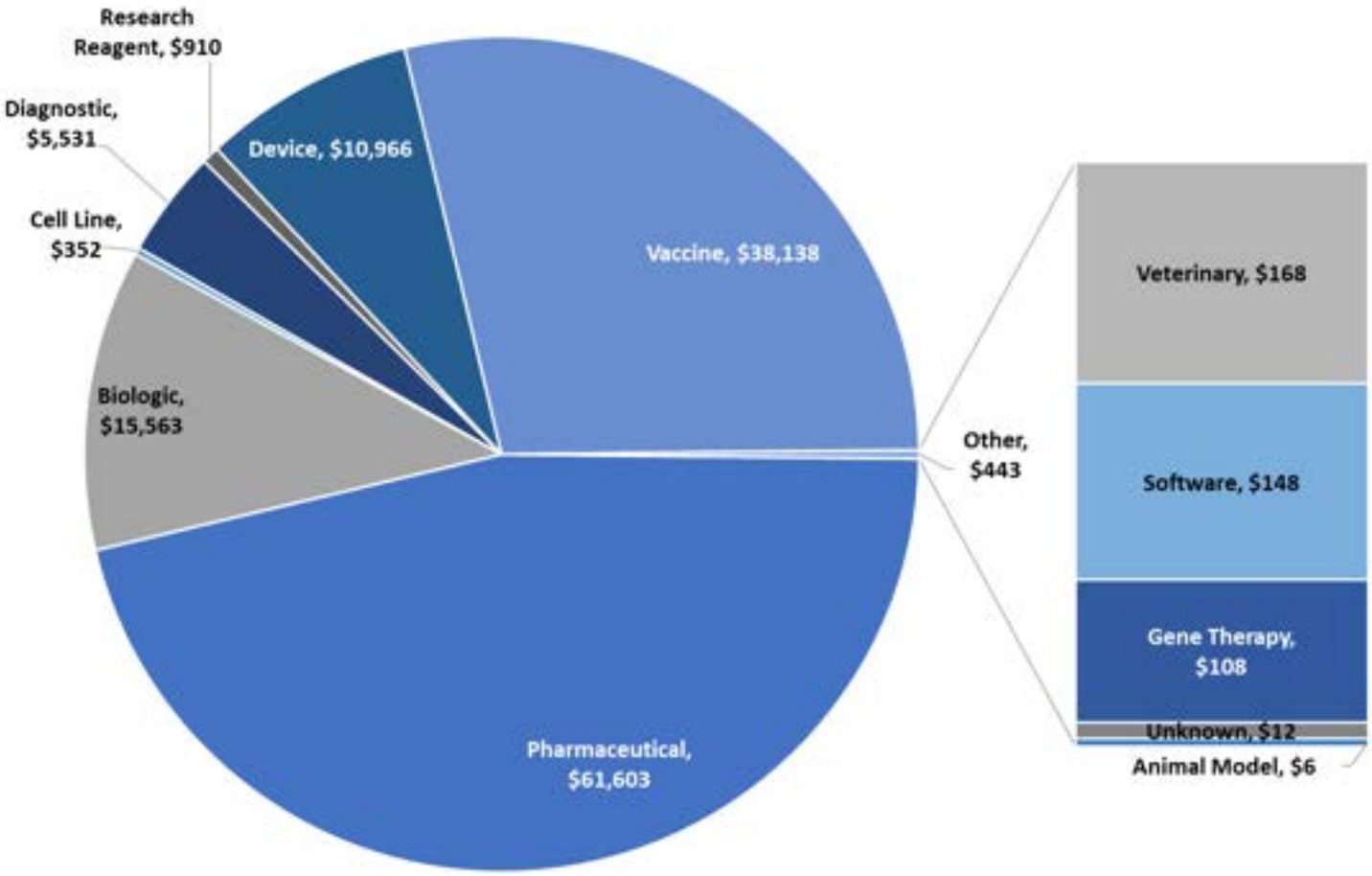


NIH Technology Licenses by Product Category: Sales

Inventions are licensed from the NIH primarily by commercial firms seeking to integrate those technologies into new products. Most products are biomedical in nature (pharmaceuticals, vaccines, devices, etc.). However, since the NIH conducts research across a wide range of fields encompassing a variety of purposes, some of the licenses were intended for use in more esoteric products. Examples include laboratory equipment (centrifuges), software for medical systems (such as Magnetic Resonance Imaging), and some veterinary products (including vaccines for dogs and cattle).

Figure 6 shows the relative share by product category of the commercial sales revenue generated by these products for licenses executed from approximately 1980 to 2021. This set of licenses produced reported sales of over $133.5 billion during this period. As might be expected given the nature of the pharmaceutical market, that class of products garnered the highest sales, constituting 46% of the total across all categories. The top-selling product in this category, Velcade, generated over $28 billion in sales by itself. Vaccines were the next highest, at 28.6%, led by the product Comirnaty (the COVID-19 vaccine produced by Pfizer and BioNTech. Biologics contributed 11.7% of total sales, and medical devices constituted 8.2%.

Figure 6: Distribution of Total Sales Income by Product Category for Licenses from 1980 through 2021, in $millions

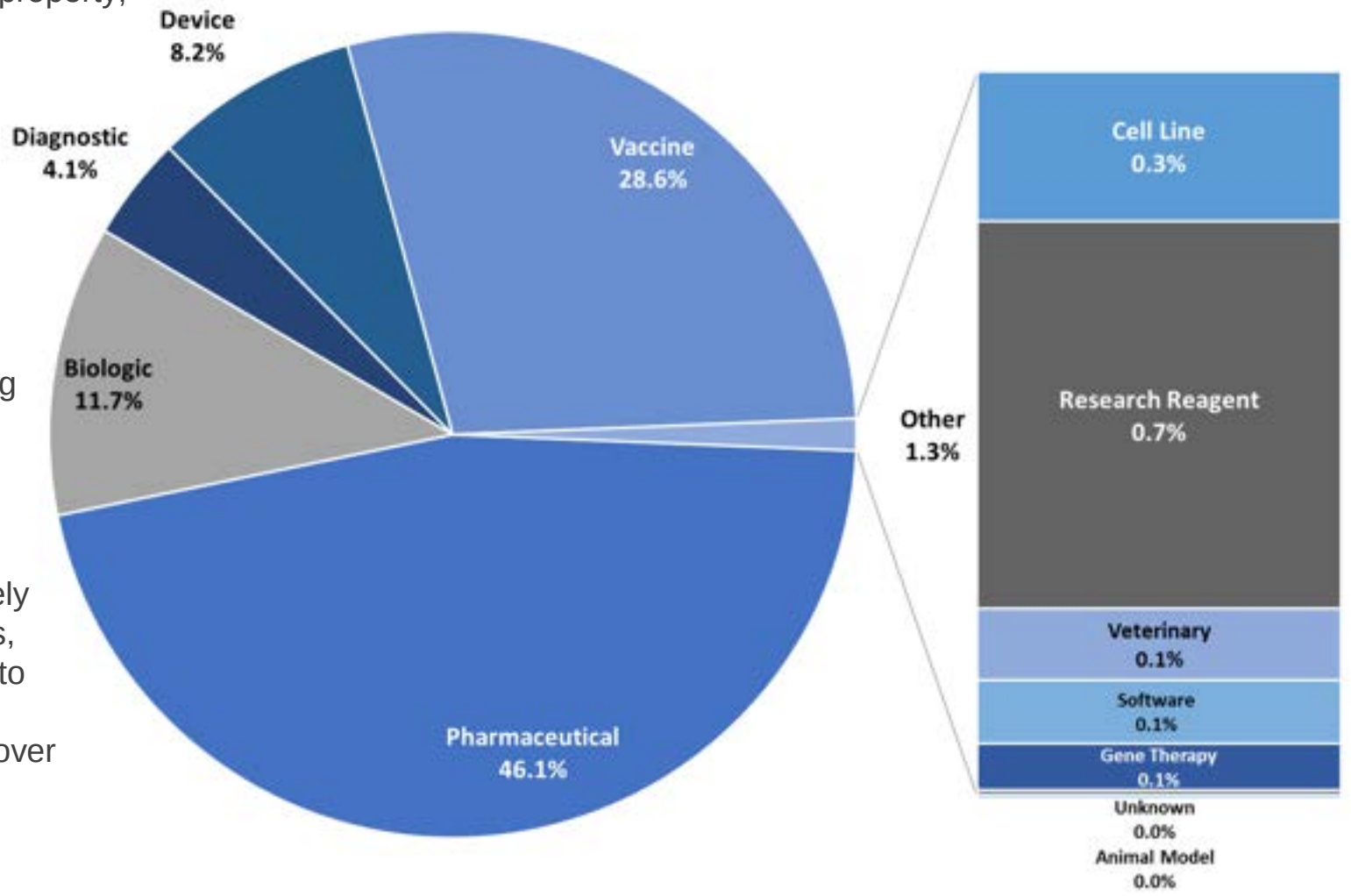


NIH Technology Licenses by Product Category: Royalties

The licenses executed by the TTOs generate income directly for the NIH in the form of royalties. Under the terms of each license, the licensee is generally required to pay the NIH an upfront amount for access to the intellectual property, and then may be required to make additional lump-sum payments upon achieving certain milestones in the commercialization process (e.g., completing Phase 1 or Phase 2 clinical trials, achieving FDA approval). After the product is launched on the market, the licensee pays the NIH a royalty, usually calculated as a percentage of the gross sales generated by the product over the life of the license. The license term varies, and is often limited by the interval from license execution to the expiration date on the underlying patents.

Figure 7 shows the relative share by product category of the royalties recorded by the NIH technology transfer offices on licenses signed between approximately 1980 and 2021. Over this period, the NIH earned approximately $1.76 billion in royalty payments. As the figure illustrates, pharmaceutical technologies and other licenses related to vaccines and therapies generated the highest shares of royalties. Several drug and vaccine licenses generated over $10 million in royalties per license.

Figure 7: Distribution of Total Royalty Income by Product Category for Licenses from 1980 through 2021



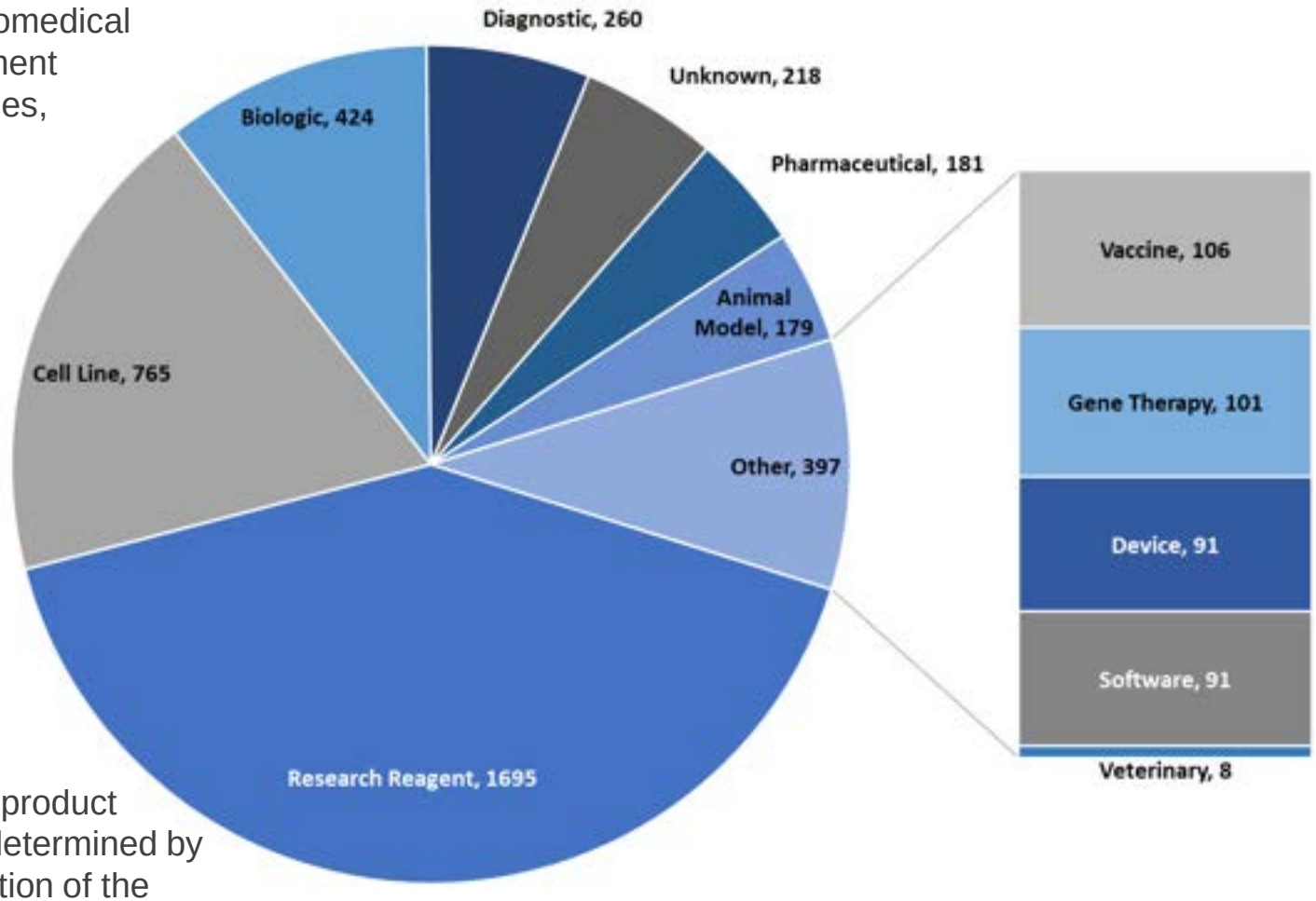
NIH Technology Licenses by Product Category: Count

In contrast to the royalty payments earned by product category, the majority of inventions licensed by the NIH cover research tools—research reagents and cell lines (see Figure 8). These technologies are used by biomedical researchers in pre-clinical research as part of the drug development process. In contrast to many licenses for pharmaceutical, vaccines, biologic, and devices, the NIH will license the same cell line or reagent to multiple licensees, and in some cases, multiple times to the same licensee.

In particular, cell lines are a key resource for biomedical R&D. They provide an in vitro model for researchers to test how a living cell might react to a particular intervention without the need to use a living cell. The Murine Colon 38 cell line has been part of 171 different licenses. Note that the NIH Office of Technology Transfer manages cell line licenses only for commercial licensees. Cell lines used by academic researchers are obtained through Material Transfer Agreements directly from the various NIH institutes and do not require a royalty payment. Animal models, such as special breeds of mice, are used for early-stage in vivo research and constitute a significant share of licenses.

Note: the TechTracS records for licenses frequently omitted the product category. In such cases, the product category of a license was determined by analyzing the technologies covered by each license, the description of the licenses found in TechTracS, and the title(s) of any inventions covered by the license.

Figure 8: Distribution of NIH Licenses by Type of Product or Technology



Impact of NIH Technology Transfer Beyond Products

As the in-house research arm of largest funder of fundamental biomedical research in the U.S., the IRP has pioneered some of the most advanced and revolutionary therapeutics and treatments. One area where the NIH has played a key leading role is FDA-approved gene therapies—e.g., Spark Therapeutics' LUXTURNA™ to treat inherited vision loss and Kite Pharma's YESCARTA™ to treat large B-cell lymphoma that is unresponsive to chemoimmunotherapy. Researchers in the NIH IRP developed the initial inventions enabling the development of these early gene therapy products and establishing that they are safe and effective.

Beyond the technologies embedded in these products, the NIH IRP has developed critical knowledge and systems for manufacturing such gene therapies, a critical capability for achieving commercial success and health impact. While gene therapies offer a new avenue for treating, preventing, and curing diseases that previously had very limited treatment option, increasing gene therapy yields and lowering production costs are prerequisites for developing gene therapies to treat diseases that affect larger populations (e.g., 100,000 doses to treat patients with a particular cancer as opposed to a rare disease with a patient population that may require 1,000 doses a year).

An example of NIH's contribution to gene therapy manufacturing is a National Heart, Lung, and Blood Institute discovery that Sf9 insect cells could be used to produce Baculovirus expression vectors. BioMarin's gene therapy, ROCTAVIAN™, used to treat severe Hemophilia A, is produced using this NIH-licensed technology. The use of insect cells, as opposed to mammalian cells, makes the gene therapy purification process simpler and more effective lowering cost and improving quality.[5]

This analysis of the impact of NIH technology transfer does not include the role of TTOs in facilitating cooperative research and development agreements (CRADAs) and other mechanisms by which NIH researchers and inventors can provide such critical know-how and expertise to licensees. Without continued collaboration with the IRP on approaches to scaling up the production of gene therapy products, the commercialization of this promising class of therapeutics is likely to stall.

Note: Cell therapy treats disease by restoring or altering certain sets of cells or by using cells to carry a therapy through the body. Gene therapy treats disease by replacing, inactivating, or introducing genes into cells.

Summary of Findings

The indicators presented here provide a multi-faceted view of the impacts of how IRP inventions, once licensed to commercialization partners, generate benefits to the U.S. and the world in accelerated and improved innovation processes, economic growth and prosperity, and enhance quality and length of life. Over a 40+-year period from 1980 to 2021, the NIH TTOs executed thousands of licenses generating billions in royalty income for NIH and multiple billions in sales for commercialization partners. These indicators show how those short-term, limited financial gains only capture a small portion of the benefits realized through NIH technology transfer. As notable examples:

- NIH technology transfer has provided key technical inputs that contributed to the development of innovative products at dozens of early-stage firms, helping to bolster the role of creative entrepreneurial teams in creating significant new therapies, treatments, and cures.
- NIH commercialization partners leveraged the technologies licensed to raise significant financial capital, justify extensive R&D investments and efforts, realizing important gains across the biomedical R&D enterprise. NIH technologies are especially significant as the basis for new research tools and other inputs that make research efforts worldwide more effective, enhancing research efficiency and enabling discoveries in new fields and topic areas.
- The revenues generated from the innovations based on NIH-licensed inventions flowed throughout the U.S. economy. Those reverberations can be seen in the thousands of jobs that were retained or created from those sales. They also generated billions of dollars in household income, tax revenues, and overall national economic growth.
- Key therapies and vaccines developed by the NIH can lead to significant improvements in the health of the U.S. population over time. For a selection of products, these indicators show that many patients have enjoyed reductions in the suffering and pain from specific diseases, gaining thousands of hours of productivity that would otherwise be spent incapacitated by illness.
- These innovations also reduce stress on the national healthcare system by keeping people healthy and out of the hospital, and also increases overall national productivity by enabling more people to work.

These gains are not achieved by technologies alone. To realize these benefits, IRP researchers, technology transfer officers, and their external licensees need to work together, engage in deep negotiations, and pursue the shared goal of bringing new biomedical innovations to the market. These impacts stem not only from discoveries and inventions, but from the commitments of time, expertise, and efforts by NIH staff and their partners in the biomedical innovation ecosystem.

2 Biomedical Innovation Impact

NIH and the Biomedical Innovation Ecosystem

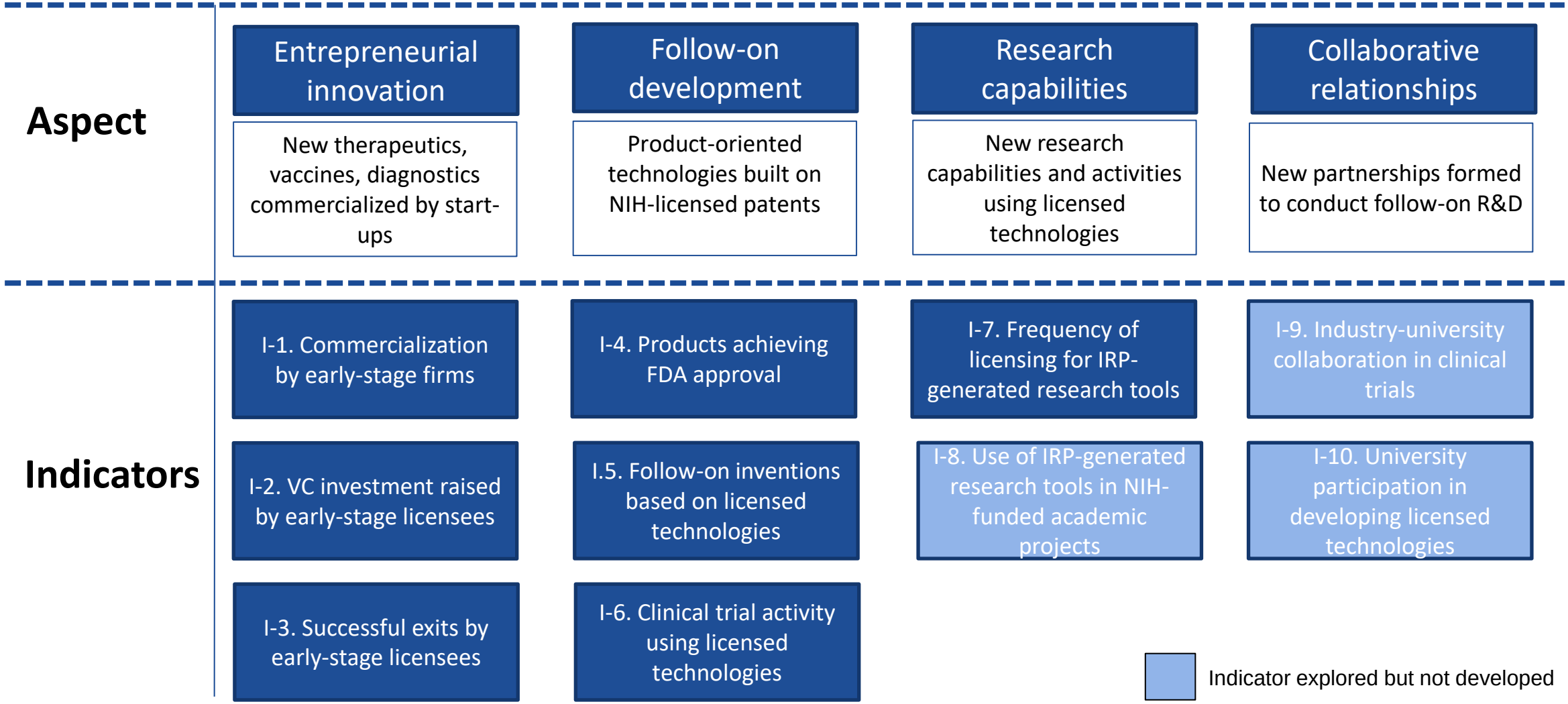
As the largest single funder of fundamental biomedical research in the U.S., the NIH is a key driver of R&D at universities and private firms dedicated to improving human health. The collection of organizations and institutions engaged in developing biomedical innovations are often characterized as members of an "ecosystem." Like a natural ecosystem, the biomedical innovation ecosystem has no single authority directing all of its members. Instead, the participants create their own relationships and negotiate transactions based on their immediate needs, resulting in a complex, self-organizing set of interconnected networks that converts fundamental scientific discoveries and inventions into treatments and therapies that are delivered to healthcare providers and patients.

Within the NIH, the IRP generates intellectual property (IP) and related knowledge that are key inputs to the overall biomedical R&D enterprise. The technology transfer offices at NIH oversees the portfolio of IP that results from IRP research activity. By licensing that IP out to firms, the IRP provides the knowledge and concepts that feed into the R&D pipeline of private firms. The TTOs also play a key role in managing the outputs of collaborative research conducted by IRP staff with scientists at universities, research institutes, and firms. The evidence of impact on biomedical innovation can be seen in four aspects, as illustrated in Figure 9 (next page):

1. Early-stage firms are one of the most important sources of biomedical innovation, especially as large pharmaceutical firms have reduced spending on laboratory research and instead acquire promising new drug candidates through mergers and acquisitions. Many early-stage firms have advanced IRP-licensed technologies towards commercialization, which enables them to raise private capital to fund that work and eventually generate financial returns through public stock offerings or by mergers and acquisition offers.
2. Since the technologies developed at NIH are pre-commercial, licensees need to invest significant resources to bring them to market. This is especially true for drugs and related products that require clinical testing to achieve regulatory approval. This follow-on R&D investment can be seen in the development of additional related technologies at firms, and by clinical trial activity leading to (and extending beyond) approval by the U.S. Food and Drug Administration (FDA).
3. The research tools developed at the IRP (cell lines, reagents, and animal models) are utilized by a wide range of biomedical laboratories to develop and test new drug candidates.
4. The IRP also enables the creation of new collaborative research relationships with universities and firms to develop additional inventions.

Analytical Model for Biomedical Innovation Impact

Figure 9: Key Aspects of IRP Technology Transfer Impact on the Biomedical Innovation System



2.1 Biomedical Innovation Impact Indicators

NIH Intramural Research and Early-Stage Companies

The biomedical and biotechnology industry is one of the most R&D-intensive industries in the U.S.[6] It is also an industry characterized by high risk, high cost, and a lengthy regulatory process to bring new products to market. The industry has shifted over time to an open innovation model in which companies invest both internally in R&D to develop new products and externally in technology scouting to acquire new products through licensing, strategic partnerships, and acquisitions of other companies.

Companies, federal government labs, like the NIH Intramural Research Program (IRP), universities, nonprofit research institutions, and individual inventors are sources of biomedical innovation. Startup companies (less than 5 years), early-stage companies (less than 15 years)[7], and established companies (more than 15 years of age and differentiated by revenue, employment size, and ownership, e.g., private or public) are all active in commercializing new biomedical and biotechnologies.

The NIH IRP supports entrepreneurial innovation through research, discovery, and licensing of NIH technologies. In RTI's analysis of the Top 150 NIH licenses by cumulative product sales from 1980-2021, 55 of the NIH-licensed technologies were commercialized by early-stage companies. The successful commercialization of these NIH-licensed therapeutics, devices, diagnostics, regents, cell lines, contributed to the product portfolios of these early-stage companies, helped them raise private investment (e.g., private equity, venture capital, etc.), and have supported revenue generation and growth. Forty-one of the 55 (74.5%) early-stage companies that received VC or private equity investment have had successful exits via initial public offerings or M&A activity, to date. Fourteen early-stage companies, at the time of NIH license, are private, revenue-generating companies.

Note that the NIH Office of Technology Transfer licenses technologies to both early-stage and established companies. Not all licenses result in a commercialized product due to a mix of technical, market, and business factors. This indicator is limited to analyzing the role of NIH IRP and early-stage companies in the commercialization of some of NIH's biggest successes as measured by cumulative product sales through December 31, 2021.

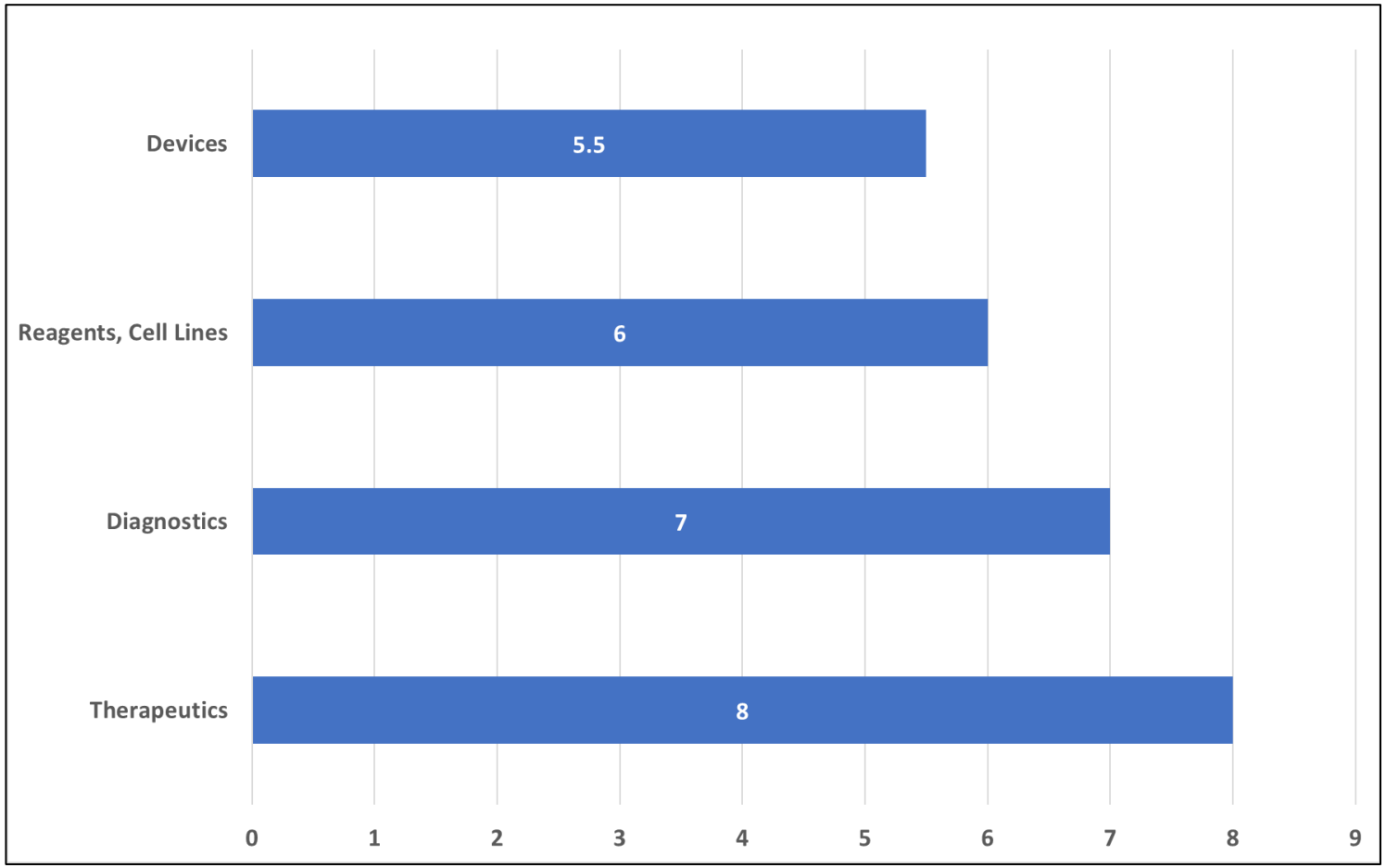
Company Age at Time of NIH License

The mean age of early-stage companies at the time of the NIH license (which contributed to a commercialized product) was 6.8 years, and the median age was 7 years (see Figure 10). Of these firms, those commercializing therapeutic products tended to be the most mature at time of license.

Although there were only a small number of firms that commercialized devices, they tended to be lower in firm age than those in other categories. However, firms in this category illustrate issues that may affect the analysis of early-stage licensees. One device licensee, Angiotech, licensed the technology for the drug-eluding stent. However, it sublicensed the technology to a large firm, Abbott, which brought the actual device (Taxus) to market. Another licensee, Brainsway, was founded specifically to commercialize the licensed technology, so the firm was effectively 0 years old at the time of license.

The firms represented in this chart spanned the entire age range from 0 to 15 years, with the majority being 5 to 10 years old at date of license.

Figure 10: Top 150 NIH Licenses by Sales:
Median Age of Early-Stage Companies by Product Category, 1980-2021



Note: Company age is measured as years between company founding and effective date of NIH license.

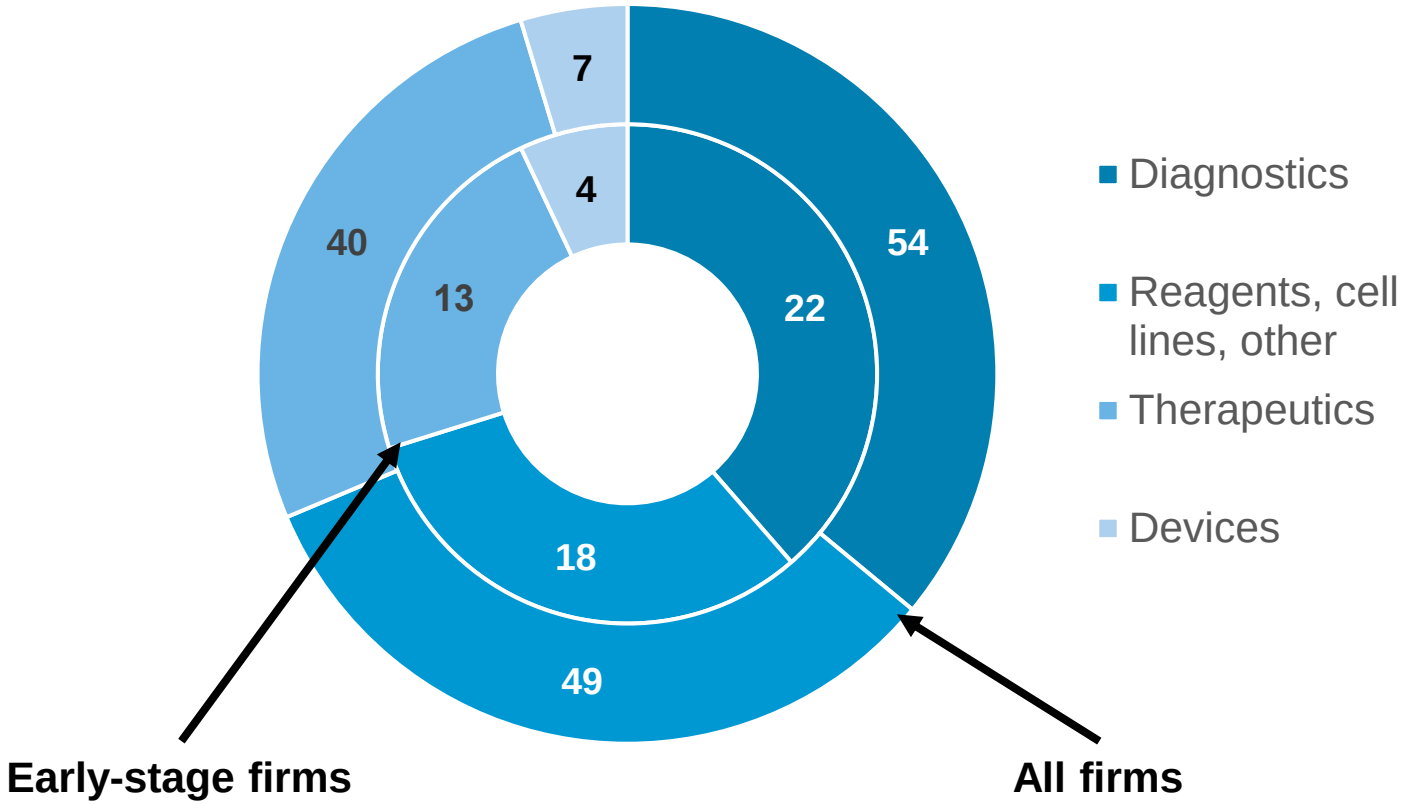
Top-Selling Products Commercialized

Among NIH's top 150 technology licenses measured by cumulative sales, 57 products were commercialized by early-stage companies. Notable examples of early-stage licensees include:

- **Diagnostics:** Virologic (Monogram Biosciences), Vysis, Cambridge Biotech
- **Therapeutics:** Millennium Pharmaceuticals, MedImmune, BioNTech
- **Cell Lines, Reagents:** BD Pharmingen, Clontech Laboratories, BioLegend, eBioscience
- **Devices:** Angiotech, Applied Spectral Imaging, Brainsway

The distribution of early-stage firms across product categories (the inner ring in Figure 11) is not substantially different from the distribution for all licensees regardless of firm age. Firms producing diagnostics were slightly more prevalent among early-stage firms (constituting about 40% of the total), while those producing therapeutics (drug, vaccines, and biologics) were slightly less prevalent (about 32.5% of the total).

Figure 11: Top 150 NIH Licenses by Sales: Presence of Early-Stage Firms vs. All Firms by Product Category, 1980-2021



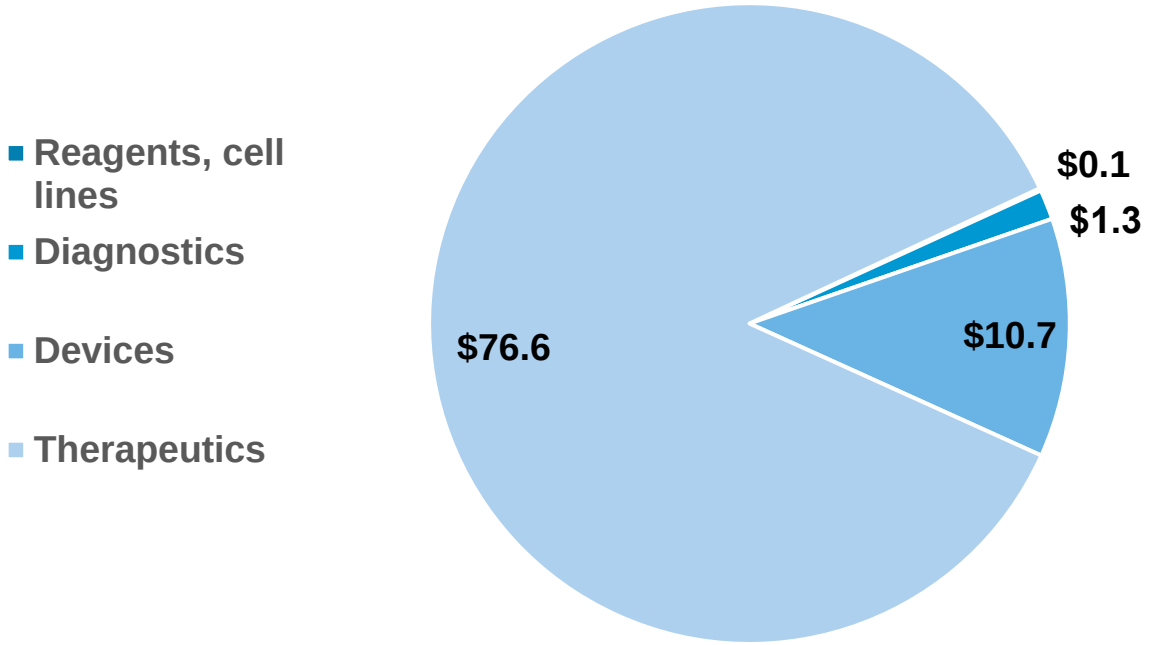
Distribution of Reported Product Sales for Early-Stage Licensees

Early-stage companies reported $88.7 billion in cumulative product sales stemming from NIH-licensed products from 1980-2021, shown in Figure 12. Similar to the overall pattern in sales by product category, the substantial majority of sales were generated by firms producing therapeutics ($76.6 billion, or 86.3% of the total). Devices accounted for 12.1% of sales, while diagnostics were about 1.5% and licenses to early-stage firms related to reagents and cell lines were only 0.1% of the total.

The table shows the wide range in products sales across and within product categories. The top-selling therapeutic generated over $28 billion in sales, while the top sales in reagents and cell lines was $15 million, differing by a factor of over 1,000. Within categories, the highest variance is in diagnostics, where the highest-grossing product generated sales over 8 times the mean. In devices, the distribution is skewed substantially by the top-selling product, Taxus, which had sales nearly 100 times higher than the 2nd-ranking product in that category. The influence of "blockbuster" products can be seen in Diagnostics and Therapeutics, where the 4 top-selling products for each category grossed much more in revenues than all of the other products in those categories.

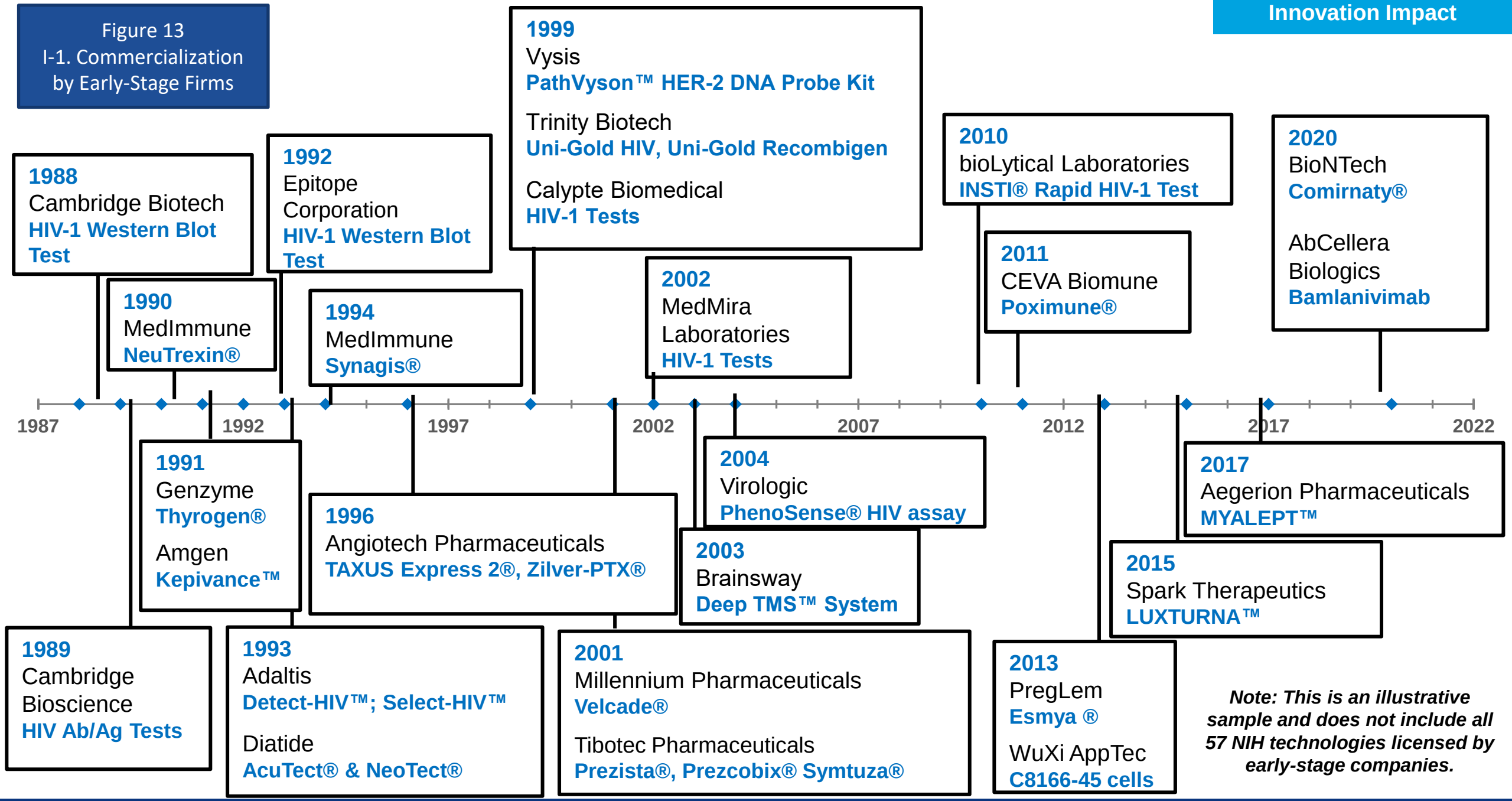
Figure 13 (next page) shows a selection of early-stage firms that developed products achieving FDA approval by year of approval.

Figure 12: Top 150 NIH Licenses by Sales:
Total Cumulative Sales (in $billions) Reported by Early-Stage Licensees by Product Category, 1980-2021



	Count of NIH licenses	Min ($M)	Max ($M)	Mean ($M)
Diagnostics	22	$3.5	$525.5	$61.1
Reagents/Cell Lines	18	$3.1	$15.4	$6.4
Therapeutics	13	$13.3	$28,130	$5,891
Devices	4	$4.1	$10,591.4	$2,677

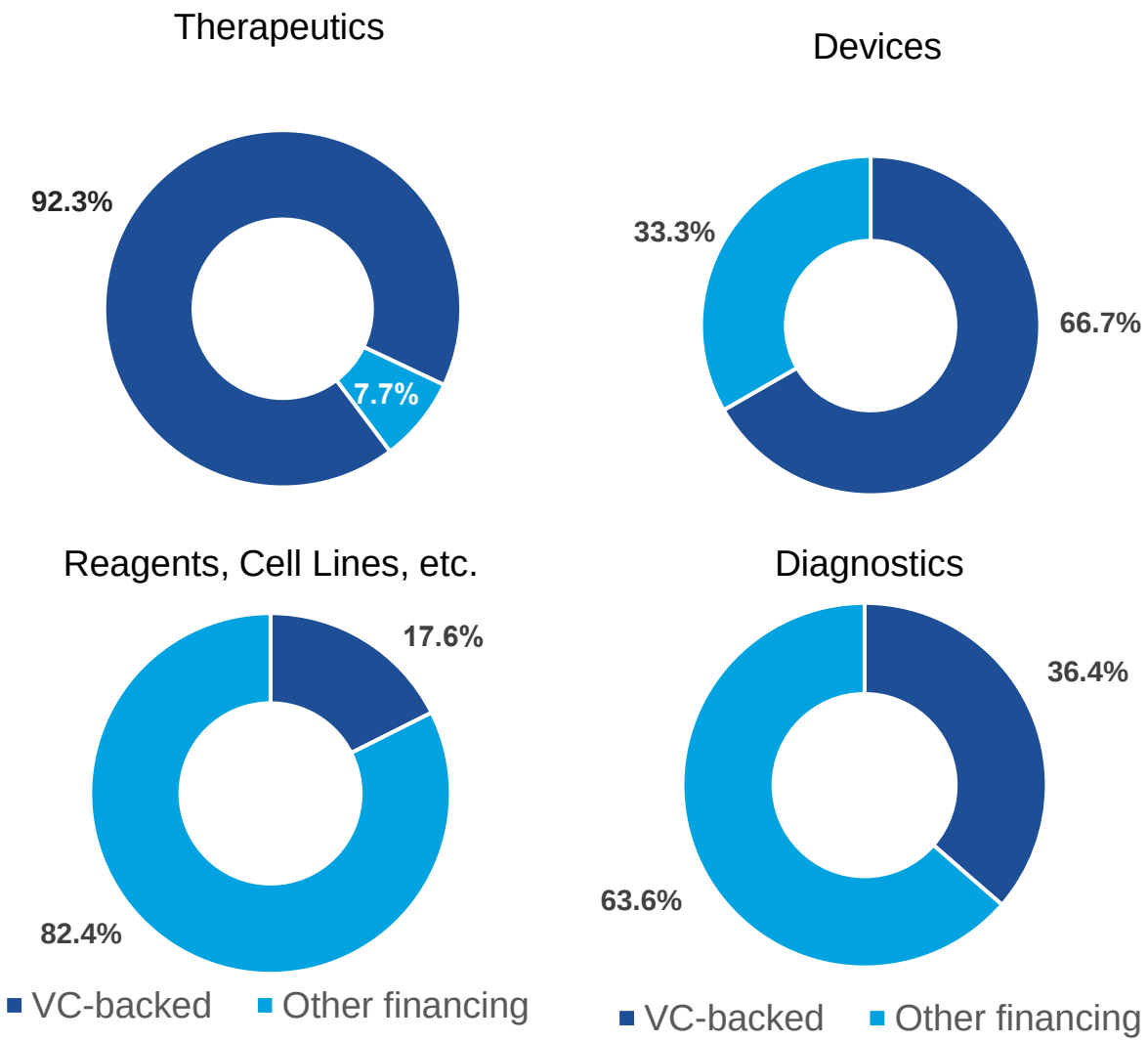
Figure 13
I-1. Commercialization by Early-Stage Firms



Note: This is an illustrative sample and does not include all 57 NIH technologies licensed by early-stage companies.

Figure 14
I-2. VC Raised by Early-Stage Firms

Share of Early-Stage Firms Backed by Venture Capital by Product Category



Privately-held firms are typically financed by private equity investors, who make their investments on behalf of high-value funding sources (such as pension funds, insurance firms, sovereign wealth funds, and high net work individuals). In later years, these firms can be self-financing through the profits earned on products and services. Standard private equity investors tend to avoid backing very risky start-ups. Those emerging firms instead draw capital from venture capital funds, who promise disproportionate returns on investment by managing their portfolios of target start-ups very carefully.

In keeping with that pattern, early-stage firms targeting therapeutic products are considered very risky due to the high rate of failure and the exorbitant cost of conducting clinical trials to achieve FDA approval. Over 92% of early-stage firms in this category received at least some venture capital to fund product commercialization. Devices are considered less risky, primarily because many of those products do not require extensive FDA scrutiny before entering the market and the total investment required is lower. Reagents and diagnostics have more consistent success and revenue patterns, so those firms can find non-VC investors more readily.

Figure 15
I-3. Successful Exits by Early-Stage Firms

For early-stage, privately-held firms, equity shareholders have few options for converting their ownership stake into liquid assets (primarily cash). Realizing a return on the capital invested requires that the firm achieve an "exit," where equity is converted into tradeable shares. The primary exit mechanisms are initial public offerings (issuing public shares) and acquisition of the early-stage company by another firm.

41 of the 55 early-stage companies among the Top 150 NIH licensees by product sales achieved successful exits. More than half (22) held initial public offerings (IPOs) and 19 were acquisition (see Figure 14). Some of the firms that went public were subsequently acquired, but our analysis focuses on the initial exit event. Note that for all US venture-backed firms, no more than 15% of firms achieving an exit event in typical year do so via an IPO.

Firms commercializing therapeutics were most likely to exit via IPO, in nearly 80 percent of cases. The remainder were acquired by other firms, mostly pharmaceutical manufacturers. Device firms used IPOs in 66% of cases, although this statistic may not be generalizable due to the small number of firms in this category. Diagnostic firms were split more evenly, with nearly half exiting via IPO and about 25 percent existing via acquisition. Early-stage firms commercializing reagents and cell lines were either acquired or were able to remain privately-held.

Exit Channel of Early-Stage Licensees in the Top 150 Products by Sales, by Product Category 1980-2021

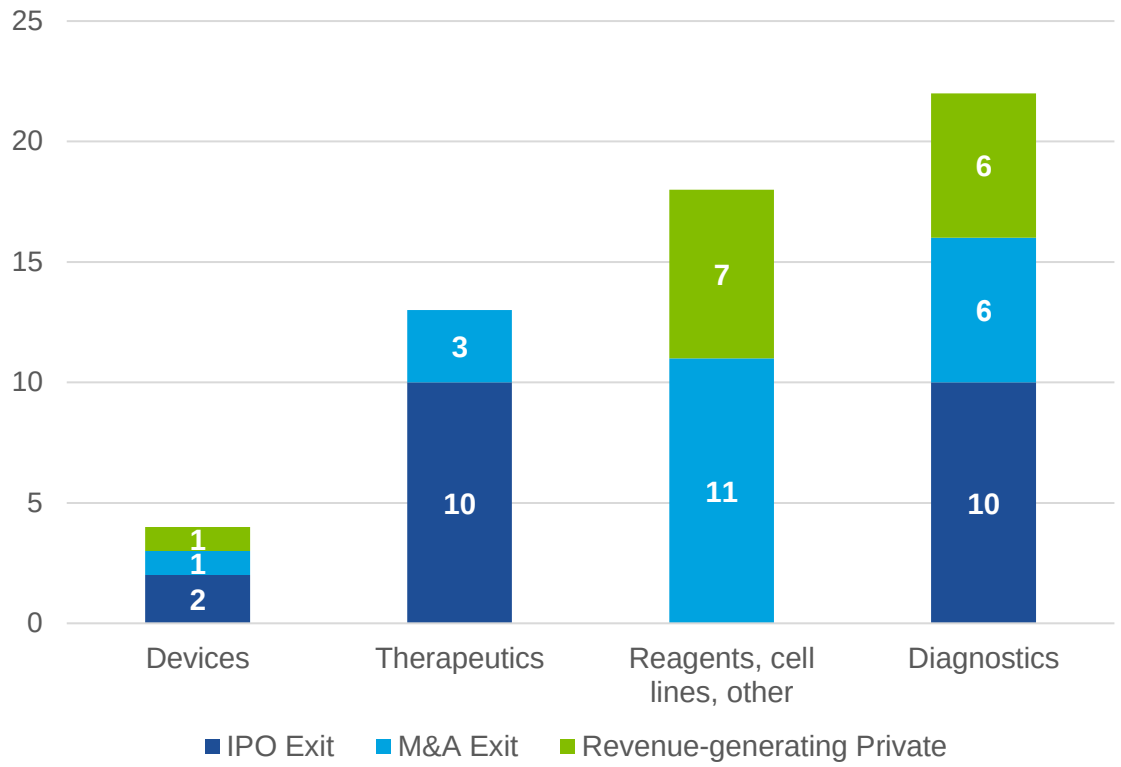
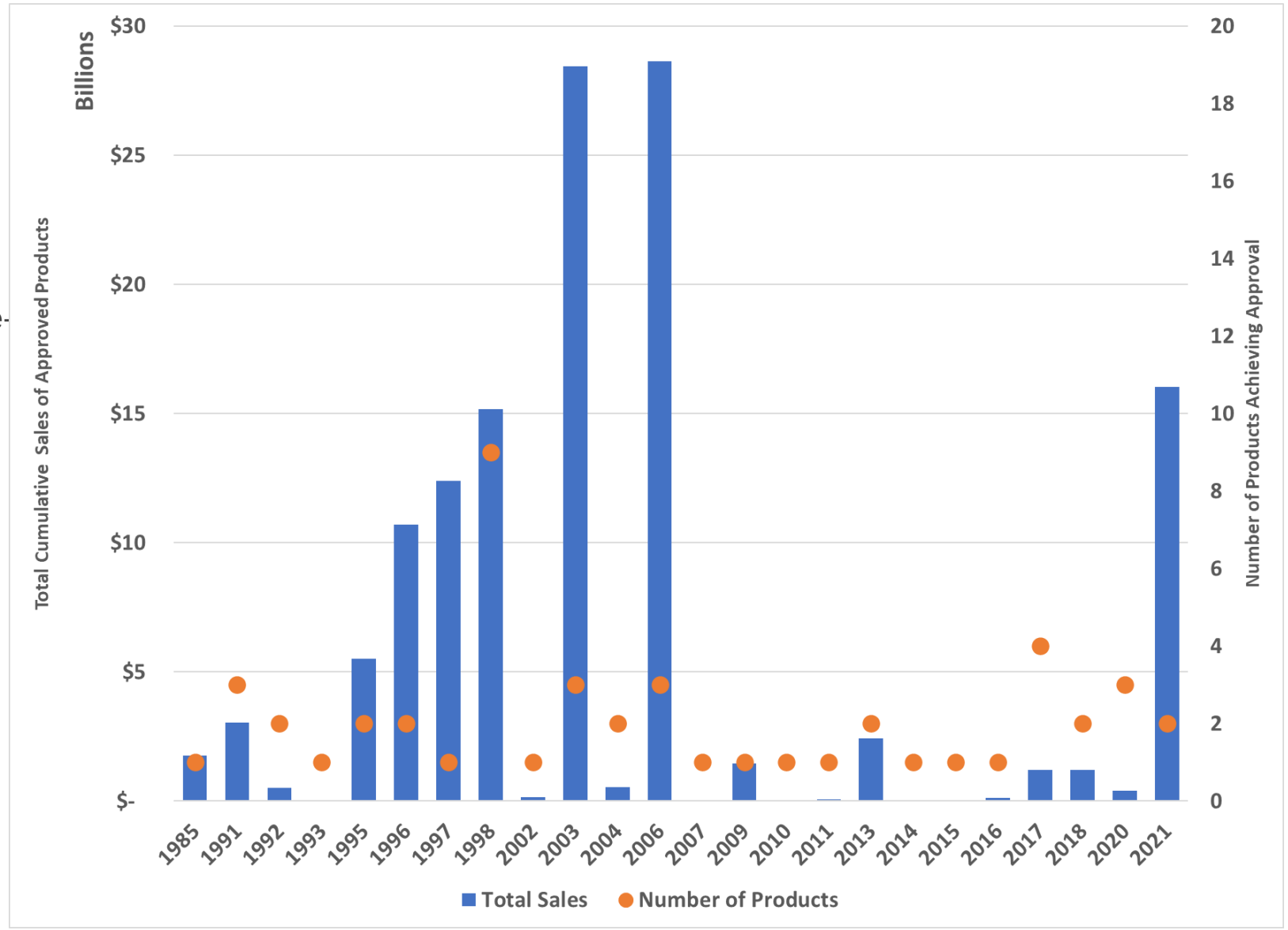


Figure 16
I-4. FDA-Approved Products Based on Licensed Technology

Among the 100 top-selling products based on technologies licensed from the NIH, at least 50 were approved by the FDA. The other 50 include products marketed outside the U.S. not requiring FDA approval and products that are not subject to FDA approval (e.g., research tools, certain over-the-counter medications, consumer medical products). Indicator I-4 (Figure 16) shows the number of products receiving FDA approval by the year of approval (data points, measured on the right axis) and the total sales reported to NIH for products approved in that year. This indicator highlights how drug sales tend to be dominated by "block-buster" products. Some years with relatively few approved products, such as 2003 and 2006, contributed disproportionately high sales by that product.

This figure also shows that sales are not necessarily a function of the number of years a product is on the market. 11 products were approved between 1985 and 1996, but their total sales amount to less than the total sales of the 3 products approved in 2003.



Interval from License to FDA Approval for Selected Products

Figure 17 presents a view of the data in Indicator I-4 (Figure 16) but focusing on the lag time between license execution and FDA approval. This figure shows that the timeline from license to approval can vary across products, and even within product categories. One key factor behind this image is that the date of execution for a license may fall well after the actual technology transfer takes place, due to occasional administrative or legal delays. Still, this figure shows that the rapid approval of Comirnaty, the Pfizer-BioNTech vaccine for COVID-19, is not the only product that received relatively rapid approval.

Figure 17: Interval Between Effective Date of License and Date of FDA Approval for Selected Top-Selling Products Based on Licensed Technologies

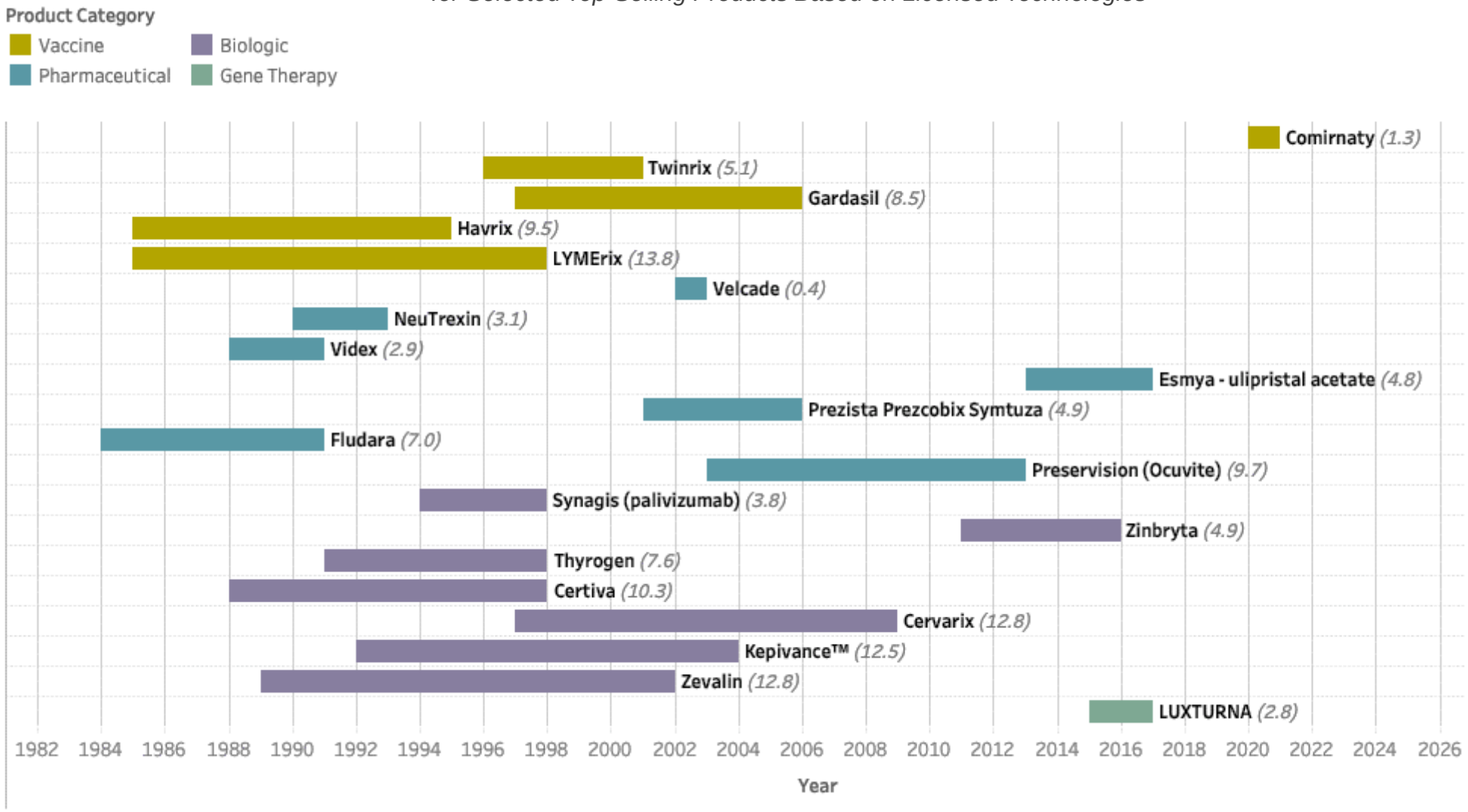


Figure 18
I-5. Follow-on Technology Development by Licensees

As noted earlier, the technologies licensed by firms from the NIH tend to be in the earliest stages of development. Those inventions form the foundation of innovative products, but the licensee frequently needs to build upon this foundation with the development of complementary and enabling technologies. One way of measuring this is to look at patents filed by a licensee that include a citation to one or more of the NIH patents covered by that license.

Any applicant must demonstrate the novelty of the invention that would be protected by the patent. To show this, applicants cite prior patents related to the subject invention. A citation shows how a particular patented invention builds upon its predecessors. Using the PatentsView database, which stores structured patent records including citation links, we can match the U.S. patents covered under NIH licenses to the PatentsView records, and then identify all of the citing patents (filed in the U.S.) where the patent owner matches the licensee. Although not conclusive, this provides a signal that the licensee has continued to elaborate on the NIH technology.

On this chart, the licensed NIH U.S. patents are shown on the left with the number of citations to that patent by licensees, while on the right are listed the licensees who have cited each patent, and the number of that licensee's U.S. patents that cite any of the NIH patents. The same patent can be licensed multiple times to multiple licensees, producing the flows indicated by the colored bars.

This chart includes 160 NIH patents; many patent numbers are hidden due to space constraints. The most prominent licensee is IONIS Pharmaceuticals (previously ISIS Pharmaceuticals), which licensed three of the NIH's U.S. patents, and cited at least one of those patents in 578 of its own U.S. patents. Baxter, Mallinckrodt Pharmaceuticals, Novartis, and Biogen show similar evidence of follow-on invention from their licenses.

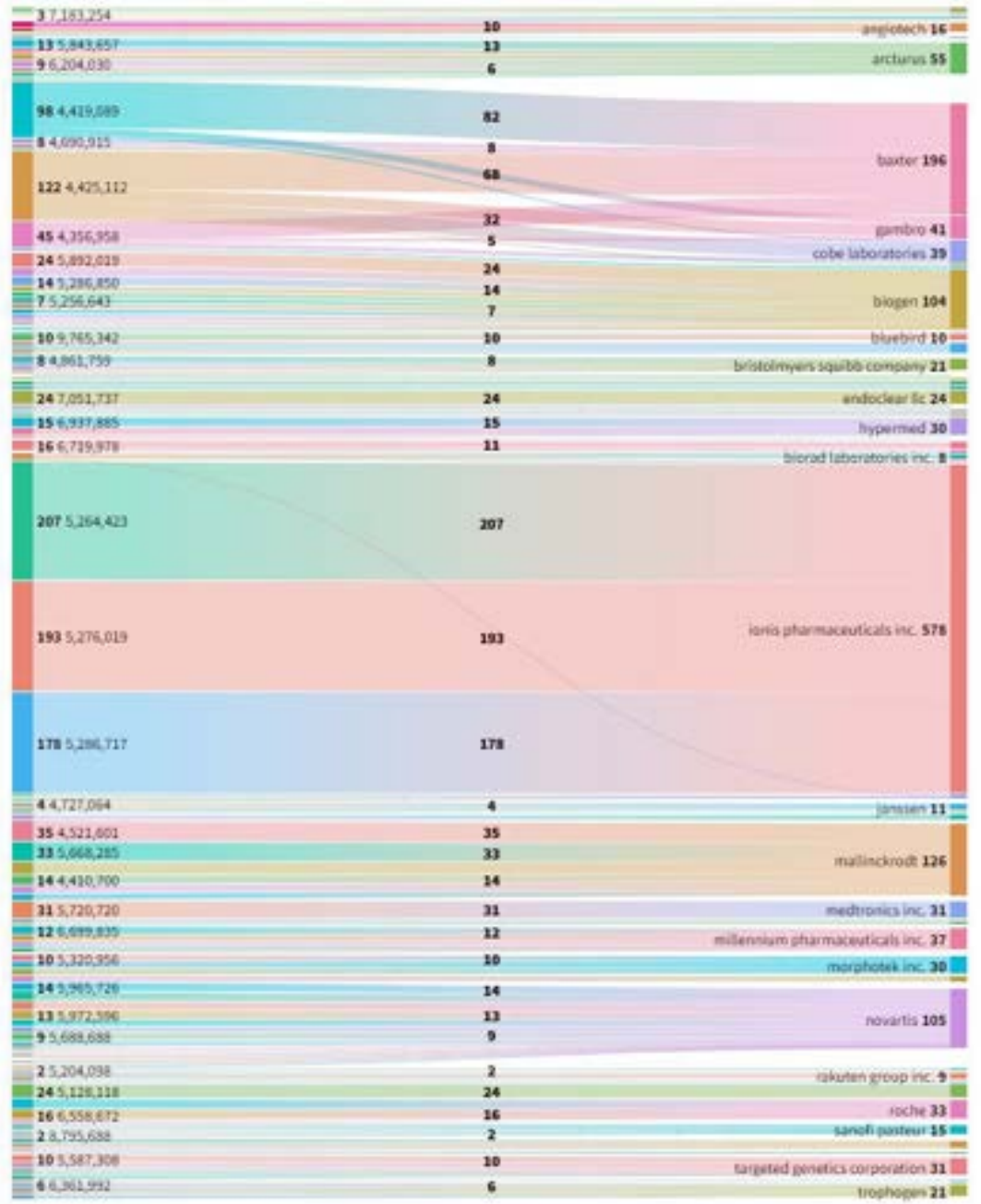


Figure 19
I-6. Clinical Trial Activity Using IRP-Licensed Technologies

Most drugs, vaccines, medical devices, and similar treatments that require FDA approval prior to marketing must undergo successive clinical trials to establish the safety and efficacy of that intervention relative to the disease or condition that it is meant to treat or prevent. Even after receiving initial FDA approval, clinical research may continue—for example, to determine if the intervention can be used by specific patient populations (e.g., children, very elderly individuals), or if the intervention works on other diseases or conditions, or to see if the intervention is more effective when used in combination with other drugs or protocols. This research may continue well past the expiration of the license, and even after the underlying patents have expired. Clinical researchers may conduct trials to determine whether older medicines have new uses or that new treatments are more effective than the older ones.

Using data from the ClinicalTrials.gov database, this indicator identifies **all** clinical trials testing a product based on NIH-licensed technologies as the intervention. As shown here, for many products, this goes far beyond those required for FDA or other regulatory approval. A search for 25 of the top-selling products from licensed technologies shows that certain products were the focus of very substantial clinical trial activity, especially Velcade (311 trials, of which 8% were Phase 4), Comirnaty (202 trials, including 46% Phase 4), and Gardasil (124 trials, including 37% Phase 4). Measured in this manner, IRP technologies contribute substantially to on-going clinical research across the world, even for research occurring well after the license period for those technologies.

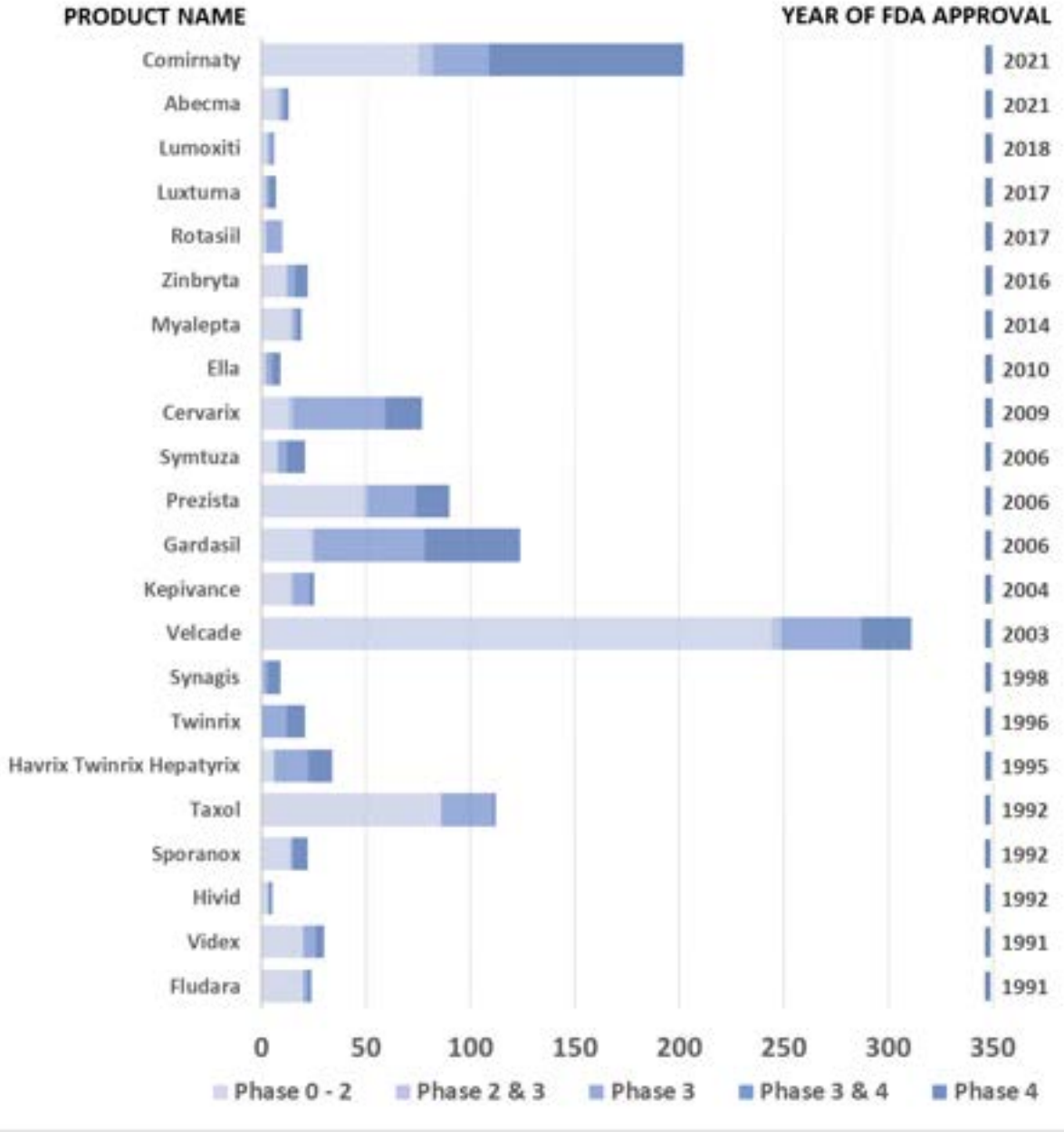
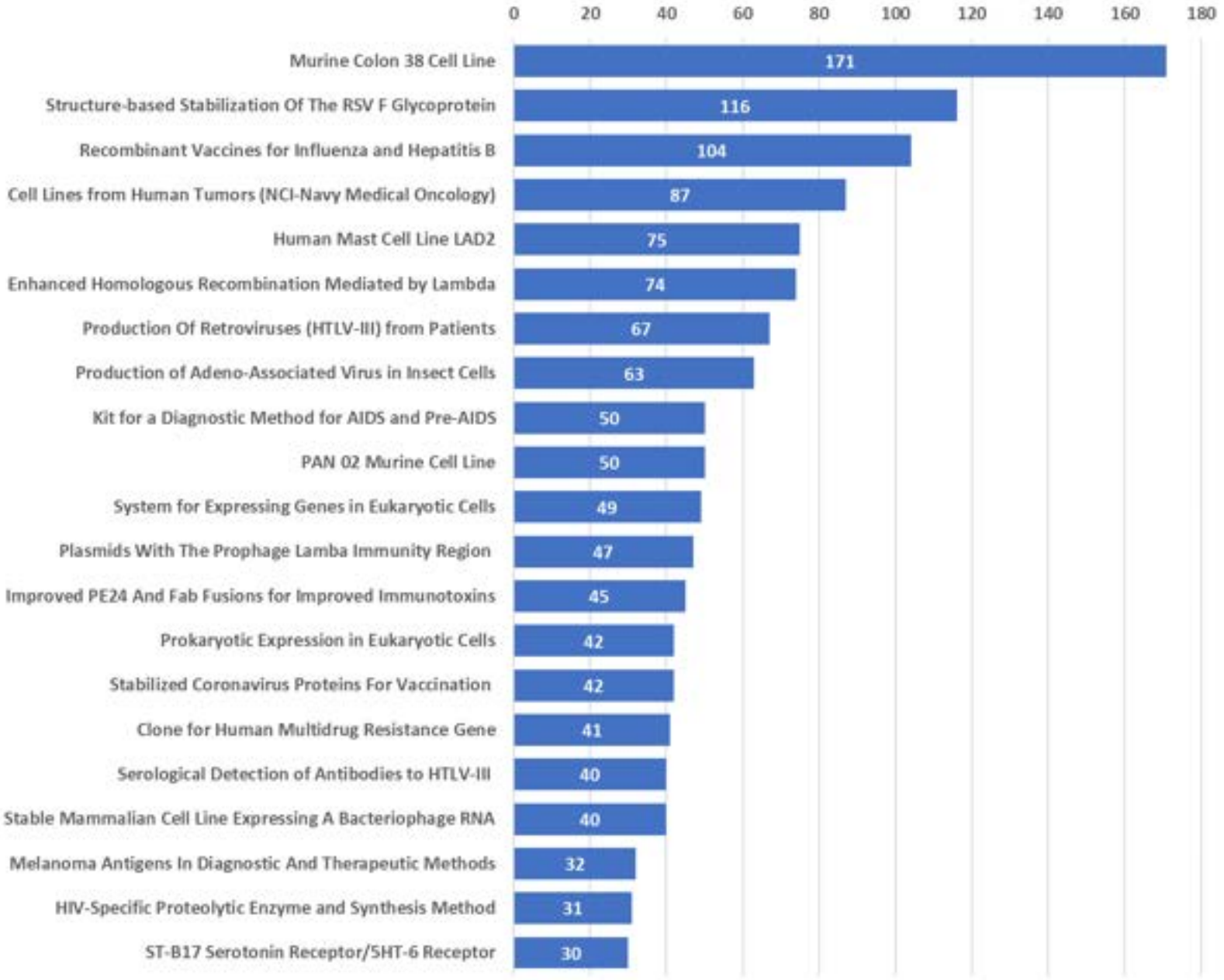


Figure 20
I-7. Frequency of Licensing for IRP-Generated Research Tools

This indicator shows the most frequently-licensed technologies covered by IRP licenses. Unlike previous analyses, this show the licenses by technology rather than product (as a single product license can encompass multiple technologies).

As might be expected from the analysis of licenses by product categories, research tools and inputs are the technologies that are most prevalent among licenses. Out of nearly 2,500 technologies listed in licenses, 21 appear in at least 30 licenses, and 41 appear in at least 20 licenses. Cell lines are the most frequently-licensed technologies. The top four cell lines together were licensed 383 times. Most of the other top technologies licensed are research reagents.

These research tools diffuse quickly through the biomedical innovation ecosystem. The Murine Colon 38 Cell Line was first licensed in 2016 and already appears on the largest number of licenses. The NCI-Navy Medical Oncology Cell Line dates back to 2008, and the LAD2 Cell Line dates to 2001.



3 Economic Impact

Estimating Economic Benefits of Commercialization

As shown in previous studies, federal laboratory technology transfer can generate significant economic benefits to the nation through the commercial innovations that originate in intramural research and are commercialized by licensees. An accurate accounting of those benefits would require interviewing all licensee firms to learn exactly how the technology licensed from the NIH contributed to product development, the precise sales for each product, the employees hired as a result of the innovation, and other sensitive information. This would entail a costly, time-consuming, and invasive data collection process.

As an alternative, economists have developed modeling techniques to estimate how changes in an industry, such as additional product sales, create ripples through the national economy. One technique, called Input-Output (I-O) modeling, takes initial money flowing into a given industry (the "inputs") and then multiplies them by coefficients based on the economic performance of that industry and its relation to other industries (suppliers or customers), and estimates the aggregate impact of those flows across industries (the "output"). A particular I-O model for the U.S. economy is integrated into a software package, IMPLAN, using federal economic, census, and labor statistics, updated annually. This model has been used in past estimates of the economic impact of technology transfer.[8]

The monitoring reports that licensees submit to the NIH TTOs include commercial sales figures for each reporting period. These reports are used to substantiate the royalties calculated by the licensee. The revenues added to the U.S. economy from new products are a key input to the IMPLAN model. After summing up the revenues in those reports by industry by year, the totals are fed into the IMPLAN software producing estimates of various aspects of economic impact, described in the boxes below.

- Industry impact, evidenced by the additional sales revenue directly generated by products based on NIH-licensed technologies
- Workforce impact, measured by the staffing positions supported by those revenues and the workers' resulting salaries and benefits
- National economic impact, including the added taxes paid to national, state, and local authorities on the new income added, and the overall addition to the Gross Domestic Product

- Direct impacts—the changes based on the revenues garnered by the licensees themselves.
- Indirect impacts—the changes generated by the licensees' additional transactions generated by the new sales, especially payments to their supply chains.
- Induced impact—the effects as the additional dollars of direct and indirect impact flow into the rest of the economy (e.g., impacts created when the licensees' employees spend their additional salaries on personal goods and services).

Analytical Model for U.S. Economic Impact

Figure 21: Key Aspects of IRP Technology Transfer Impact on the U.S. Economy

Aspect	Industry Impact	Workforce Impact	National Economic Impact
	Contribution to industry-level financial performance	Contribution to jobs and worker incomes	Total contribution to the national economy
Indicators	E-1. Sales revenue from commercialized products, by industry	E-2. Job-years attributed to product sales	E-4. Federal tax revenue attributable to product sales
		E-3. Labor compensation generated by product sales	E-5. Total tax revenue attributable to product sales
			E-6. Change in Gross Domestic Product from product sales

3.1 Economic Impact Indicators

Figure 22
E-1. Sales Revenue from Commercialized Products, by Industry

Figure 22 shows the cumulative (not annual) total commercial sales generated by products marketed by firms using the IP licensed from NIH. Sales figures are shown in 2021 constant dollars to adjust for inflation.

Although the TechTracS database contains sales figures reported by licensees, the records have two limitations. First, some licenses are structured so that reports may cover multiple years, so the sales figures in such reports cannot be attributed to individual calendar years. Second, a licensee is only required to report sales during the period when the license is active. Many products are likely to continue to accrue sales after the license period ends. This figure will be updated as we obtain data for sales of some products extending beyond their license terms.

As noted in Figure 6, the total sales of products based on NIH licenses reached over $130 billion in 2021. The sales are attributed to industries based on product categories, so sales of therapies (pharmaceuticals, vaccines, gene therapies, other biologics) constitute the majority of sales each year. The significant jump in additional sales shown for 2021 is attributable almost entirely to the sales of Comirnaty, the Pfizer-BioNTech vaccine for COVID-19.

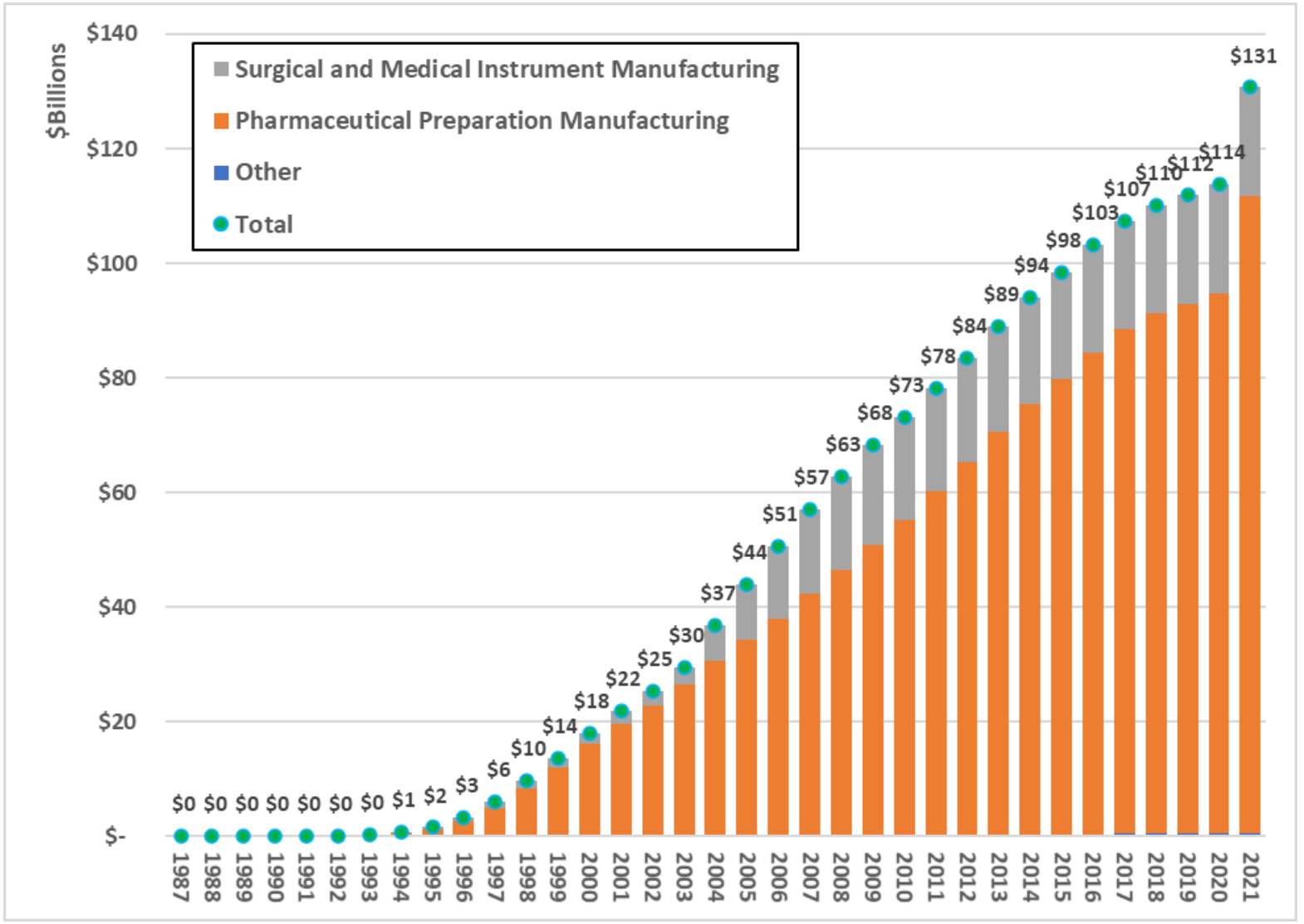


Figure 23
E-2. Job-Years Attributed to Product Sales

IMPLAN uses industry-specific sales figures to estimate the number of staff positions whose salaries would be supported by revenue from products using NIH-licensed inventions. Unlike other employment impact calculations, IMPLAN does not measure full-time equivalent (FTE) jobs.[9] Instead, it measures the number of staff positions, where any position may be part-time or full-time. This is expressed as "job-years" supported: the number of staff positions during each year whose salaries are supported by the revenues reported by licensees. The job-years include direct employment (staff at licensee firms) as well as indirect and induced employment (staff at suppliers whose products are purchased by licensees, and any other firms whose business benefits from the additional salaries covered).

Since the same job may be counted in subsequent years, this number does not reflect net new jobs. This statistic is driven by sales generated by products, based on employment patterns in each industry. From 2001 through 2021, NIH licensing contributed to an average of about 75,500 total jobs supported per year, of which 33,600 were direct jobs.

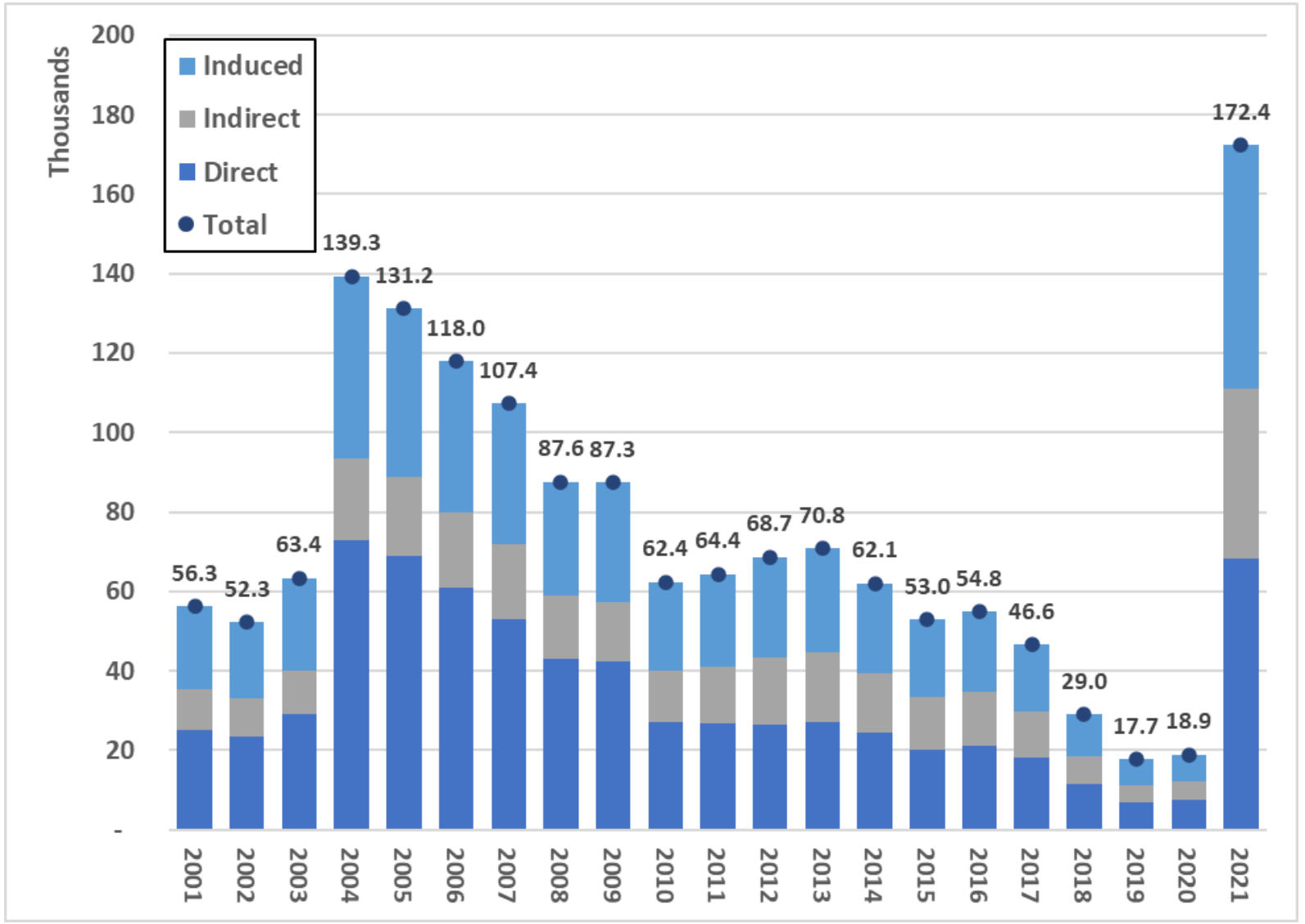


Figure 24
E-3. Labor Compensation Generated by Product Sales

This indicator measures the impact of NIH licensing activity on household incomes, both for direct employment (jobs supported at licensee firms), induced employment, and indirect employment. Based on the job-years supported calculated for Indicator E-2 and the industries to which those jobs are assigned, IMPLAN generates the total value of wages and benefits paid to workers in those jobs during the appropriate year based on occupational compensation statistics. The figures here are adjusted to constant 2021 dollars.

The industry-specific wage patterns cause this indicator to look slightly different from Indicator E-2. Since most of the job-years can be attributed to pharmaceutical manufacturing, which has higher compensation than many other industries, an increase in pharmaceutical product sales in a given year will drive a disproportionate rise in total compensation. This also creates larger variations in indirect and induced compensation.

This indicator represents the direct monetary benefit to the U.S. workforce attributed to NIH licensing activity, illustrating how those technologies enable products that create income for U.S. households.

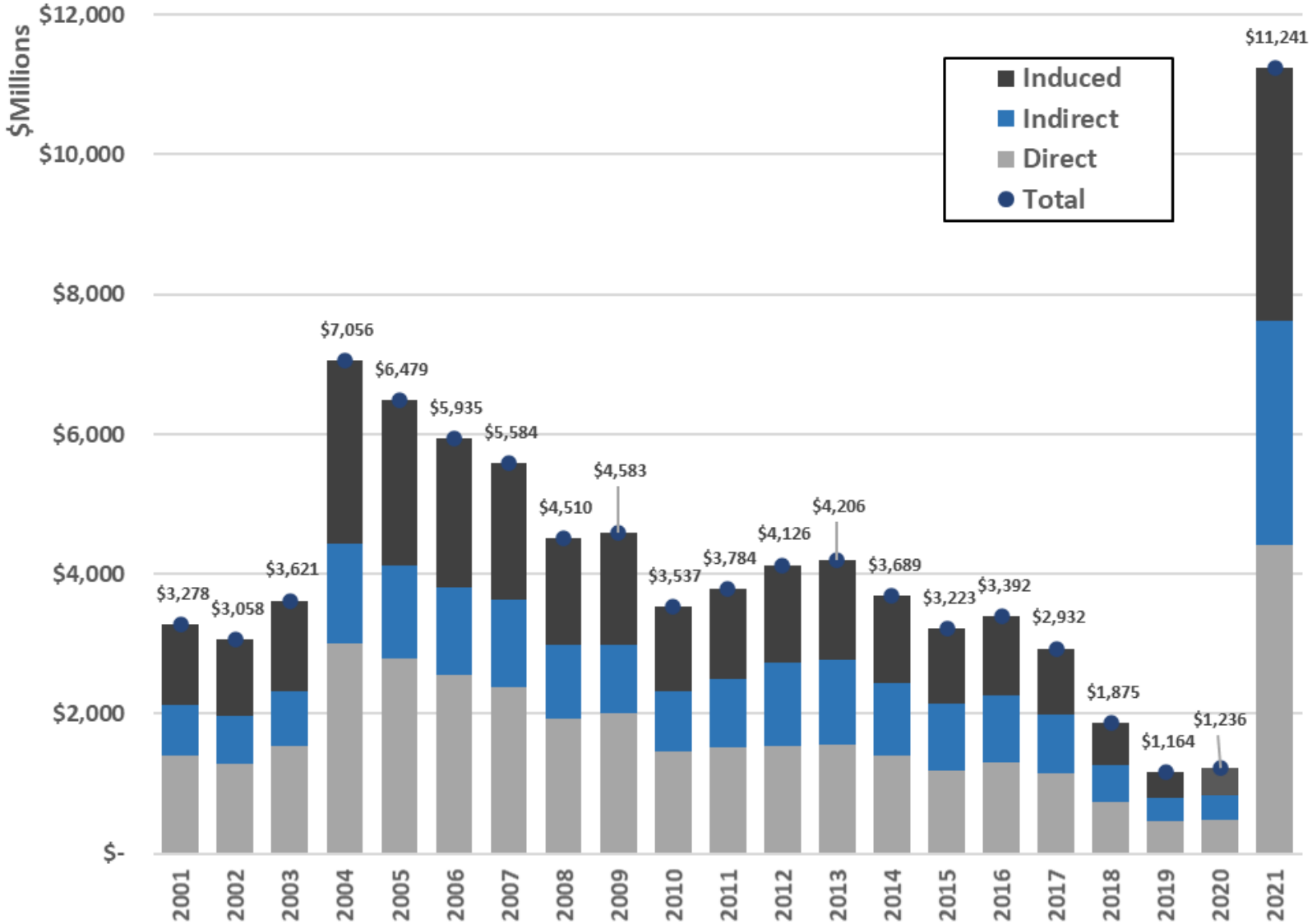


Figure 25
E-4. Federal Tax Revenue Attributable to Product Sales

This indicator shows the benefit to the federal government based on the fiscal impact of NIH-licensed technologies. The licensees selling commercialized products pay corporate income and related taxes on the income associated with that sales revenue, which are collected by the federal government. In addition, the change in employment attributed to those product sales will generate new labor income (shown in indicator E-3) which in turn generates new federal income tax paid by workers. IMPLAN calculates these estimates based on prevailing tax rates that apply to firms and workers in the affected industries. As a result, it does not measure the actual taxes paid by those firms and workers (which would require collecting data directly from the IRS).

One way to interpret this indicator is the net income to the federal government that then can be used to fund all government expenditures. Unlike licensing royalties, these tax revenues are collected directly by the U.S. Treasury. This measures a monetary benefit to the nation, as this federal tax income reduces the budget deficit each year and generates fiscal revenue that might otherwise be collected from other sources. Over this period, NIH licensing contributed to economic output that generated over $20 billion in federal taxes.

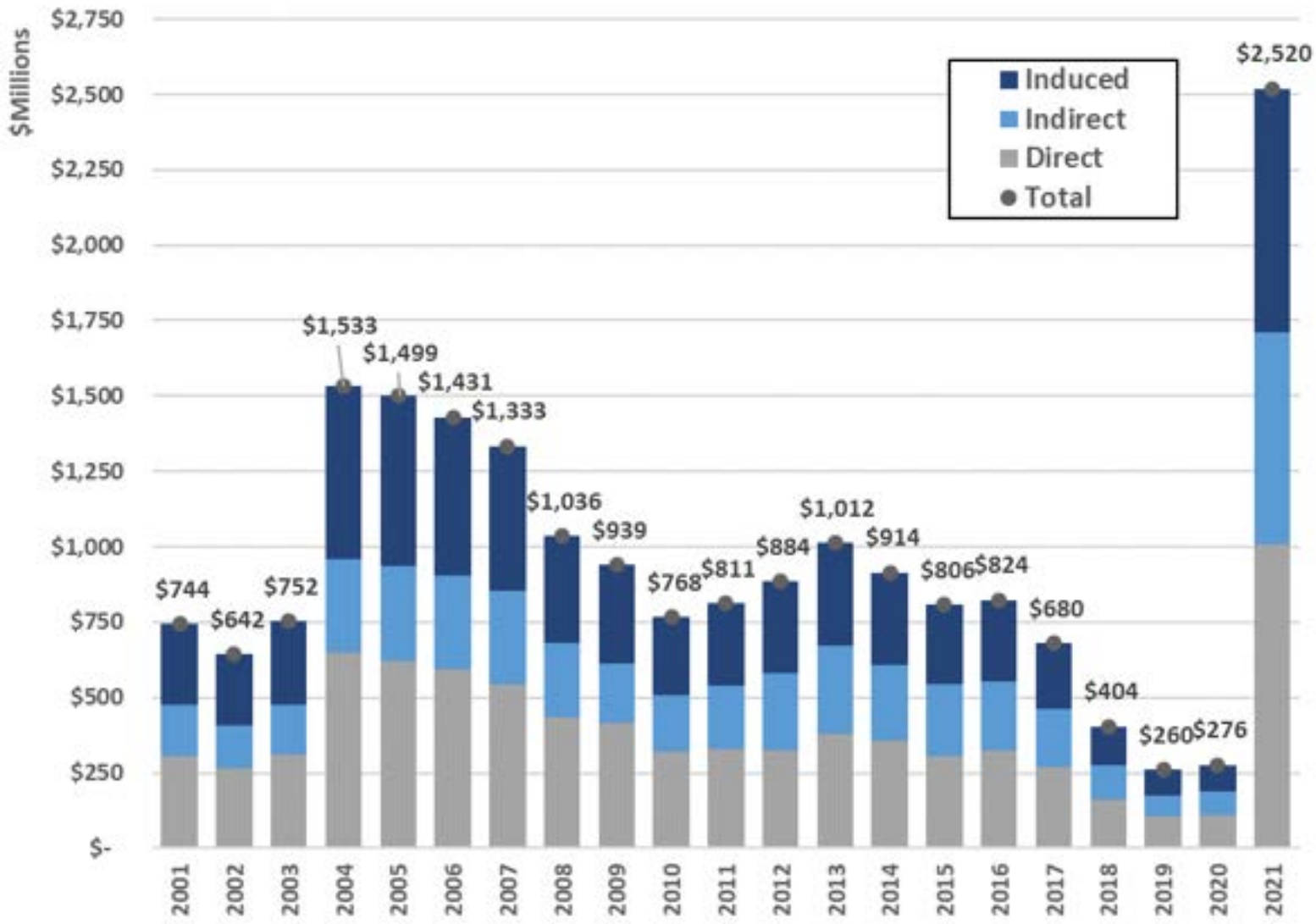


Figure 26
E-5. Total Tax Revenue Attributable to Product Sales

Since corporate and labor income is also taxed by state and local jurisdictions, this indicator provides a more comprehensive estimate of fiscal impact by summing estimates of federal, state, and local taxes paid by licensees, employees, and indirect beneficiaries of licensees' product revenue. This illustrates that NIH licensing activity has local benefits in addition to national-level benefits. Moreover, many state and local jurisdictions (unlike the federal government) charge sales taxes that would apply to at least some product sales.

This indicator uses a general estimated tax rate (which cannot account for corporate or personal tax avoidance or tax mitigation activities). In addition, the sales monitoring reports do not provide information needed to geolocate the sales earned by licensees or their products. Therefore, rather than estimating state-by-state average taxes, IMPLAN uses a single national estimate for the overall average tax rate across all states and localities.

Comparing this to Indicator E-4, the marginal benefit to nonfederal jurisdictions is substantial. For example, in 2021, estimated total taxes was more than 60% above federal taxes ($4.2 billion vs. $2.5 billion).

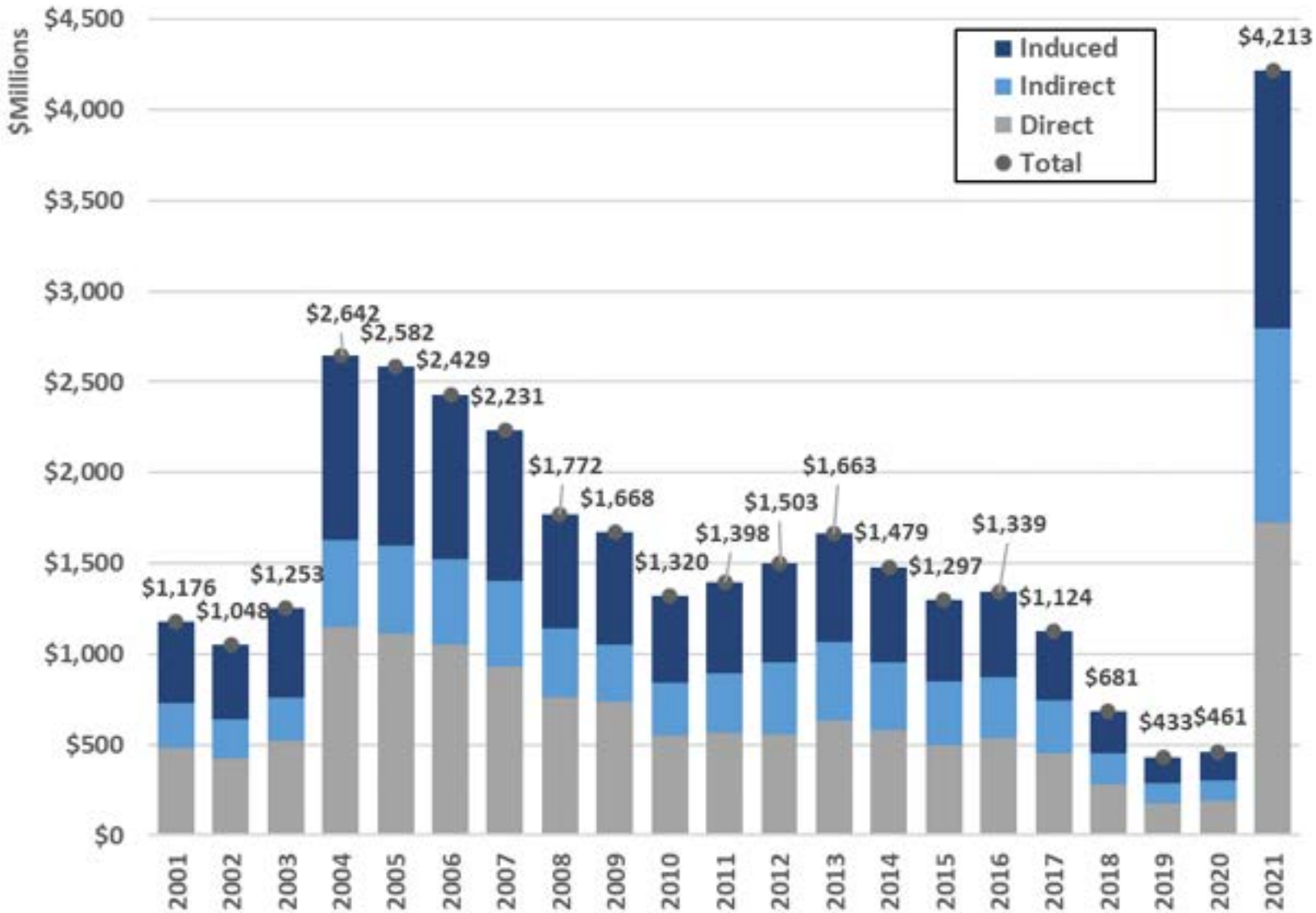
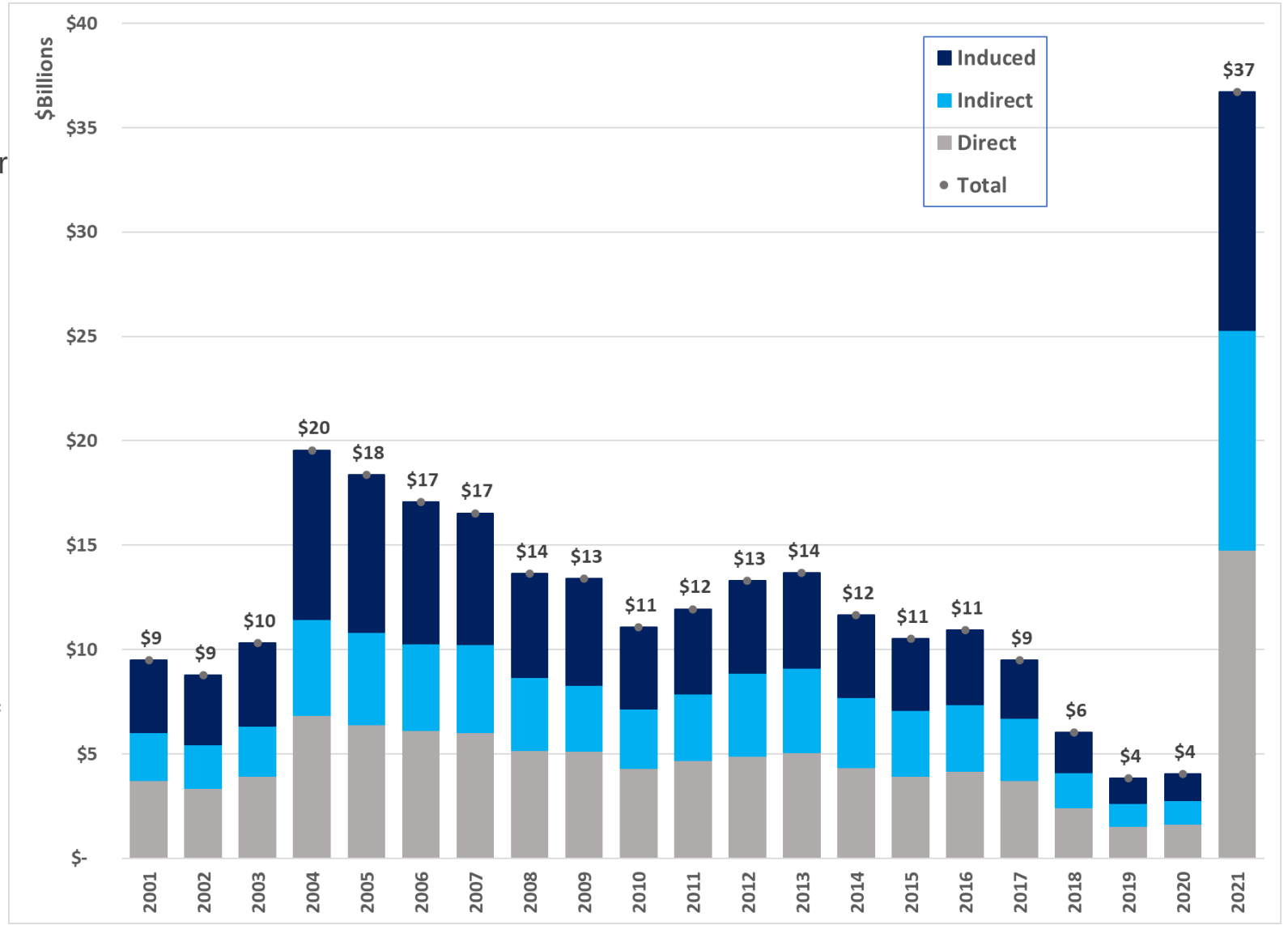


Figure 27
E-6. Change in Gross Domestic Product from Product Sales

This indicator shows how the economic activity attributed to products using NIH-licensed technologies contribute to aggregate US economic output each year (measured as Gross Domestic Product). It represents the increase in the total economic output of the US each year (i.e. the economic value added) from the sale of commercial products incorporating NIH-licensed technologies. By increasing the output and productivity of the licensees through new product development, NIH licensing improves this headline indicator of US economic performance.

The absolute contribution to GDP may seem substantial; for example, the contribution to GDP in 2004 amounted to nearly $20 billion in 2021 constant dollars. However, the U.S. GDP for manufacturing industries in that year was over $4 *trillion* dollars (not adjusted for inflation), so the relative contribution to GDP may seem minute. However, this is the impact of a single agency (NIH) working with a small subset of industries (pharmaceuticals, medical devices, and other healthcare products). Considering that NIH's licensing activities consume a small share of the NIH budget, this scale of economic impact is considerable.



4 Population Health Impact

The Role of NIH-Licensed Technologies in Population Health

For NIH technologies that contribute to the development of specific therapeutics and vaccines, we can measure how those products improved the health of the population by estimating the number of individuals/patients who received those products and by measuring impacts of medical product utilization on health care utilization, productivity (in the labor force and at home), and population-level disease burden. However, a challenge of estimating the health-related impacts of NIH technologies is that these impacts are far downstream from the innovation that spurred medical product development. To assess health-related impacts, it is important to first identify the conditions treated or prevented by those medical products that have enjoyed wide enough use to have a meaningful impact on patient and population health. Next, for each condition addressed by the medical products, we estimate disease and mortality burden and impacts on productivity and health care utilization. We examine a time period before the new medical product is approved and another after product approval. Finally, we estimate how much of the health-related improvements identified for a condition are attributable to utilization of the vaccine or therapeutic. For vaccines, which are intended to prevent future disease, a modeling approach is used to estimate the future impact of vaccinations on disease incidence and health burden. These aspects and indicators of population health impact are shown in Figure 28.

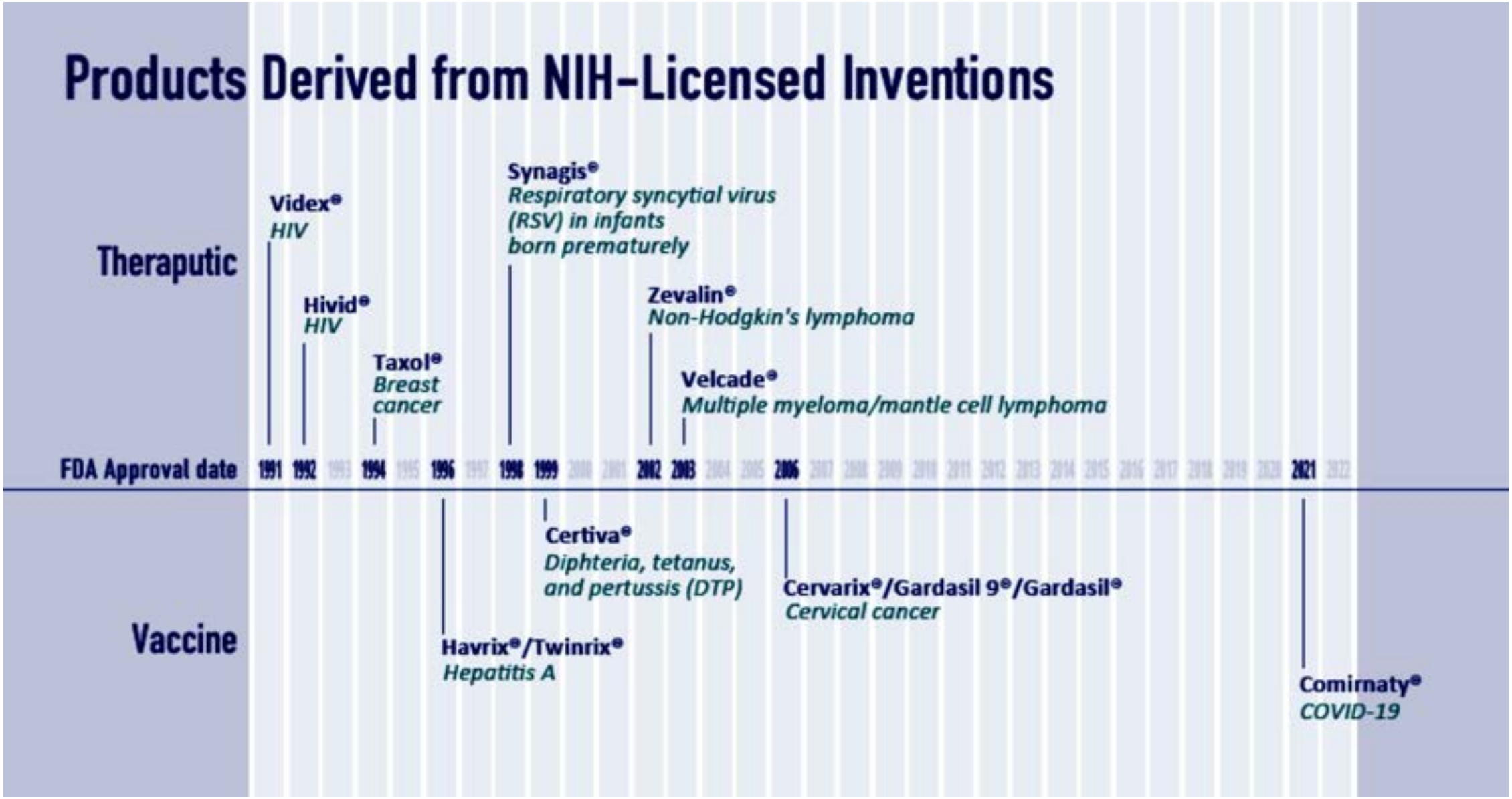
The vaccines and therapeutics considered for inclusion in the health indicators analysis were approved between 1991 and 2021 and had total commercial sales plus royalties of $200 million or more. For health indicators analyses, we focused on products that addressed conditions that could be readily identified and tracked in U.S. and global population health surveys (e.g., blood cancers, breast cancer, HIV, cervical cancer). Additionally, because it is difficult to assess how an improved formulation of an existing product affects health outcomes, we generally focused our analyses on the earliest products for a particular indication (e.g., antiretroviral treatments for HIV). The products included in health indicators analyses and the conditions addressed are shown in Figure 29.

Analytical Model for Population Health Impact

Figure 28: Key Aspects of IRP Technology Transfer Impact on Population Health

Aspect	Workforce Health Impact	Healthcare System Impact	Population Health Impact
	Productivity gains from improving household-level health outcomes	Change in demand for healthcare services and associated costs	Population-level improvements in health and mortality outcomes
Indicators	H-1. Reduction in worker absenteeism due to improved health	H-3. Change in healthcare utilization for conditions addressed by new vaccine or therapy	H-4. Reduction in disease incidence and prevalence due to new vaccines and therapies
	H-2. Increase in household productivity due to improved health		H-5. Reduction in mortality due to use of new vaccines and therapies

Figure 29: Products from NIH-Licensed Inventions for Measuring Population Health Impact



4.1 Population Health Impact Indicators

Indicators of Public Health Impact

Our focus was on generating health indicators for two products implemented between 2000 and 2019. The first was a therapeutic, Velcade®, which was approved in 2003 for the treatment of multiple myeloma and mantle cell lymphoma. The second was a vaccine to prevent HPV, a virus that is responsible for about 90 precent of cervical cancer cases. The first HPV vaccine approved for use in the United States was Gardasil® in 2006, but other manufacturers and formulations have been formulated for use since then. By focusing on these two products that were approved in 2003 and 2006, respectively, we were able to obtain sufficient pre- and post-approval data to assess the potential impact of these products on health-related burden for the indicated diseases.

For the products approved before 2000, we had limited pre-approval data available to assess the products' impacts on health, but we found evidence of declining trends in healthcare utilization to treat the conditions addressed by several of these products. For example, we saw declines in rates of hospital discharges for HIV, breast cancer, and RSV-related pneumonia, suggesting that the availability and increased use of Videx®, Hivid®, Taxol®, and Synagis® in the 1990s may have been a factor in the declines in hospitalization rates for conditions these products treated.

Before Velcade was approved in 2003, US adults with lymphoma lost an average of 18.4 days of work owing to illness or injury per year compared to only 4.5 days for workers without cancer. After approval, average days of work lost decreased by 6.1 days for workers with lymphoma, but only decreased by 0.77 days for workers without cancer. This comparison suggests Velcade may be responsible for a gain of approximately 5.3 workdays per year for lymphoma patients who were in the labor force.

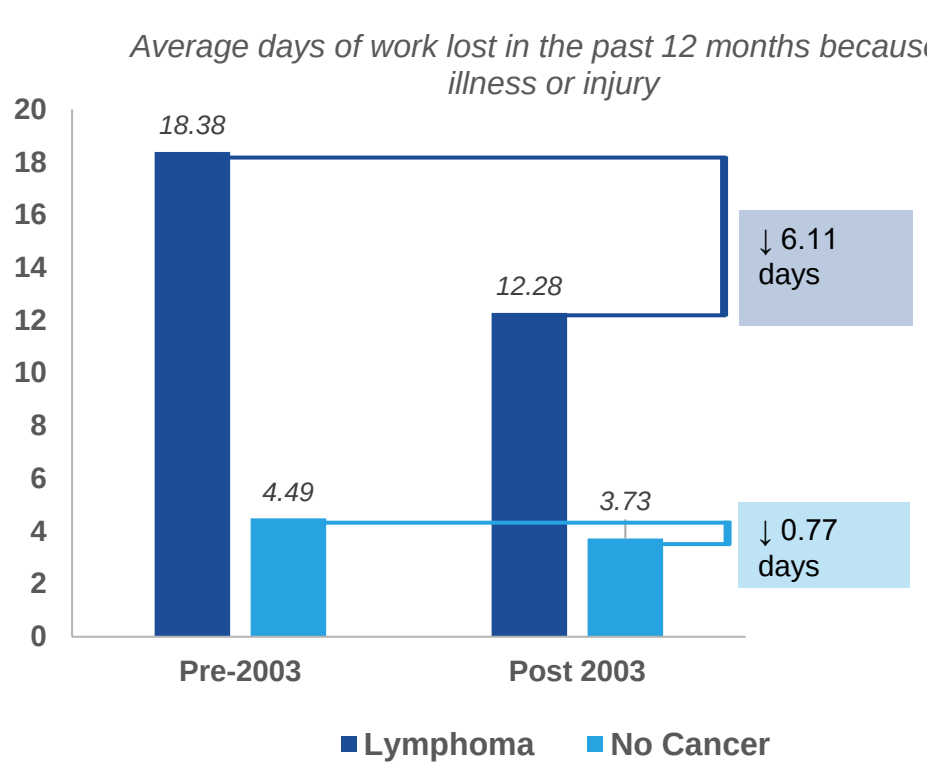
Similarly, after Velcade's approval in 2003, there was a 7.3 percentage point reduction in adults with lymphoma not in the labor force in the past 1-2 weeks, with rates of labor force non-participation declining from 59.2% to 51.9%. This is a considerable reduction in non-participation in the labor force for patients with lymphoma. Additionally, because adults who did not report a cancer diagnosis also experienced a much smaller decline in labor force non-participation (32.8% to 30.0%), findings suggests that treatment with Velcade may be responsible for increasing lymphoma patients' ability to work outside the home while undergoing treatment.

Figure 30
H-1. Reduction in Worker Absenteeism due to Improved Health

Benefits from Velcade to Treat Multiple Myeloma and Mantle Cell Lymphoma—Labor Productivity

Velcade is a targeted chemotherapy treatment approved in 2003 for multiple myeloma patients and patients with mantle cell lymphoma who had received at least 1 prior therapy. In the United States in 2019, 27,825 new cases of myeloma were reported, and 12,455 people died of this cancer. Additionally, rates of new myeloma cases are increasing; from 1999 to 2019, the age-adjusted rate of new myeloma cases increased from 5.6 per 100,000 people to 6.8 per 100,000 people.

Based on annual sales of Velcade and average annual spending of $85,000 per patient per year, we calculate 330,000 patient years of utilization, with an average of 17,400 patients using Velcade per year since its approval in 2003.



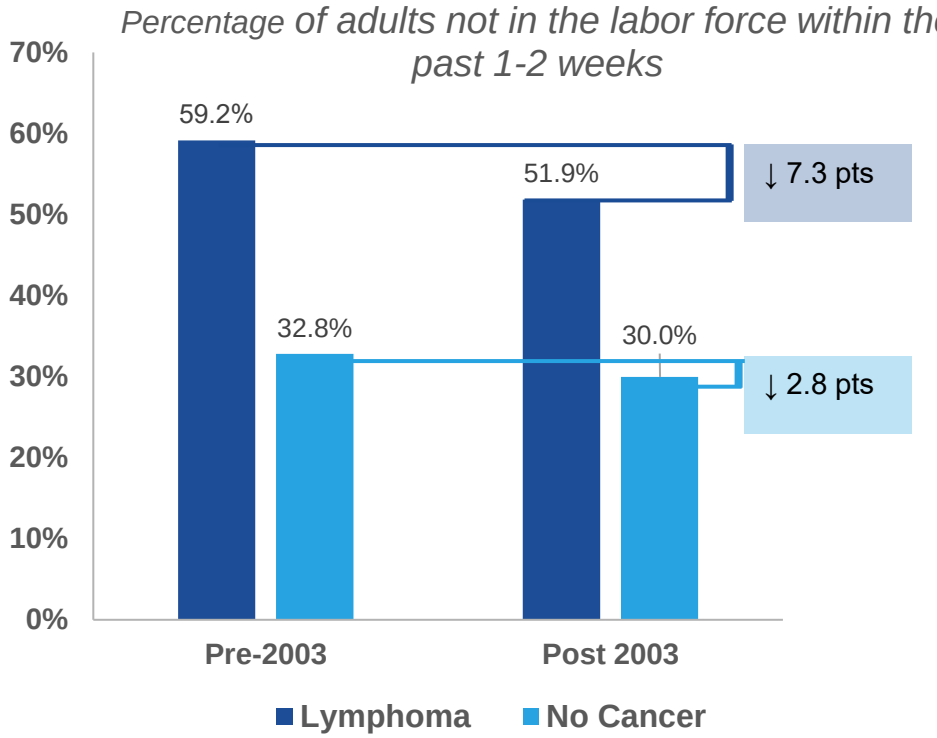
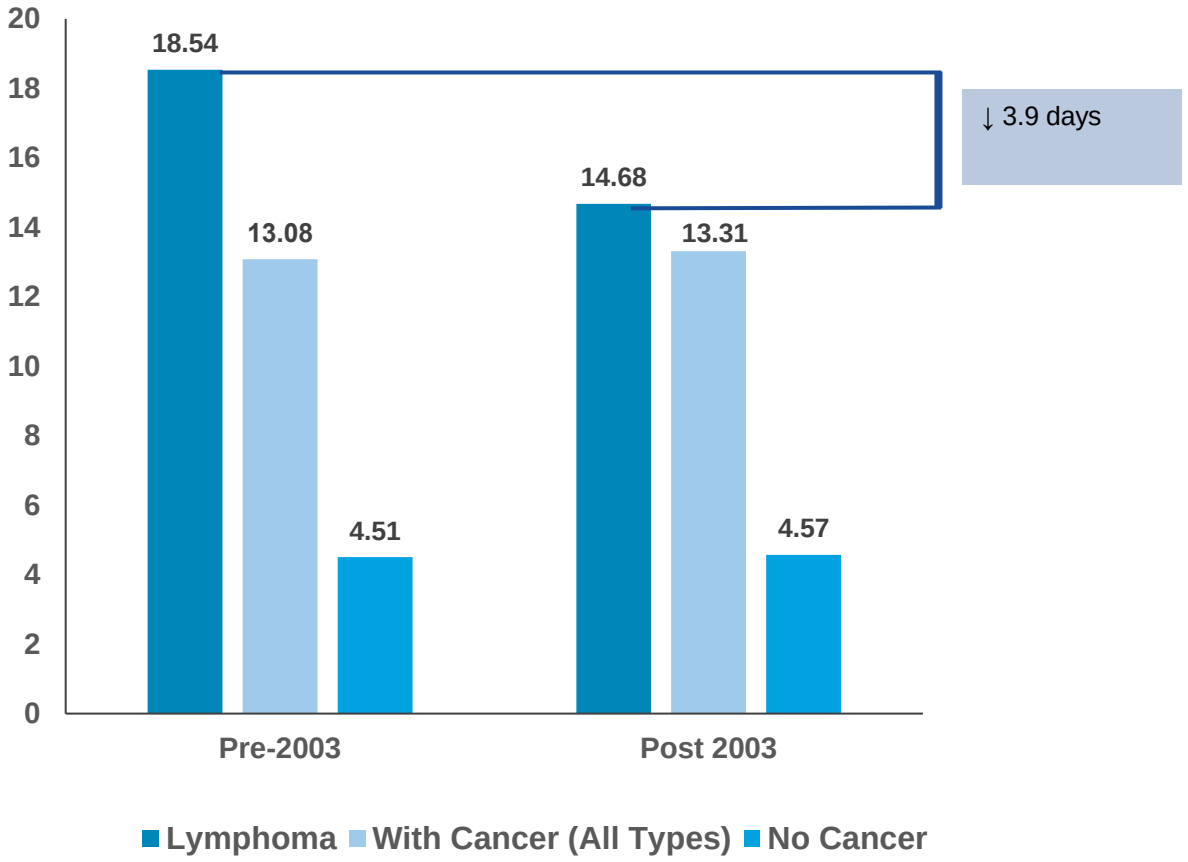


Figure 31
H-2. Increase in Household Productivity due to Improved Health

Benefits from Velcade to Treat Multiple Myeloma and Mantle Cell Lymphoma—Home Productivity

Average bed disability days in the past 12 months



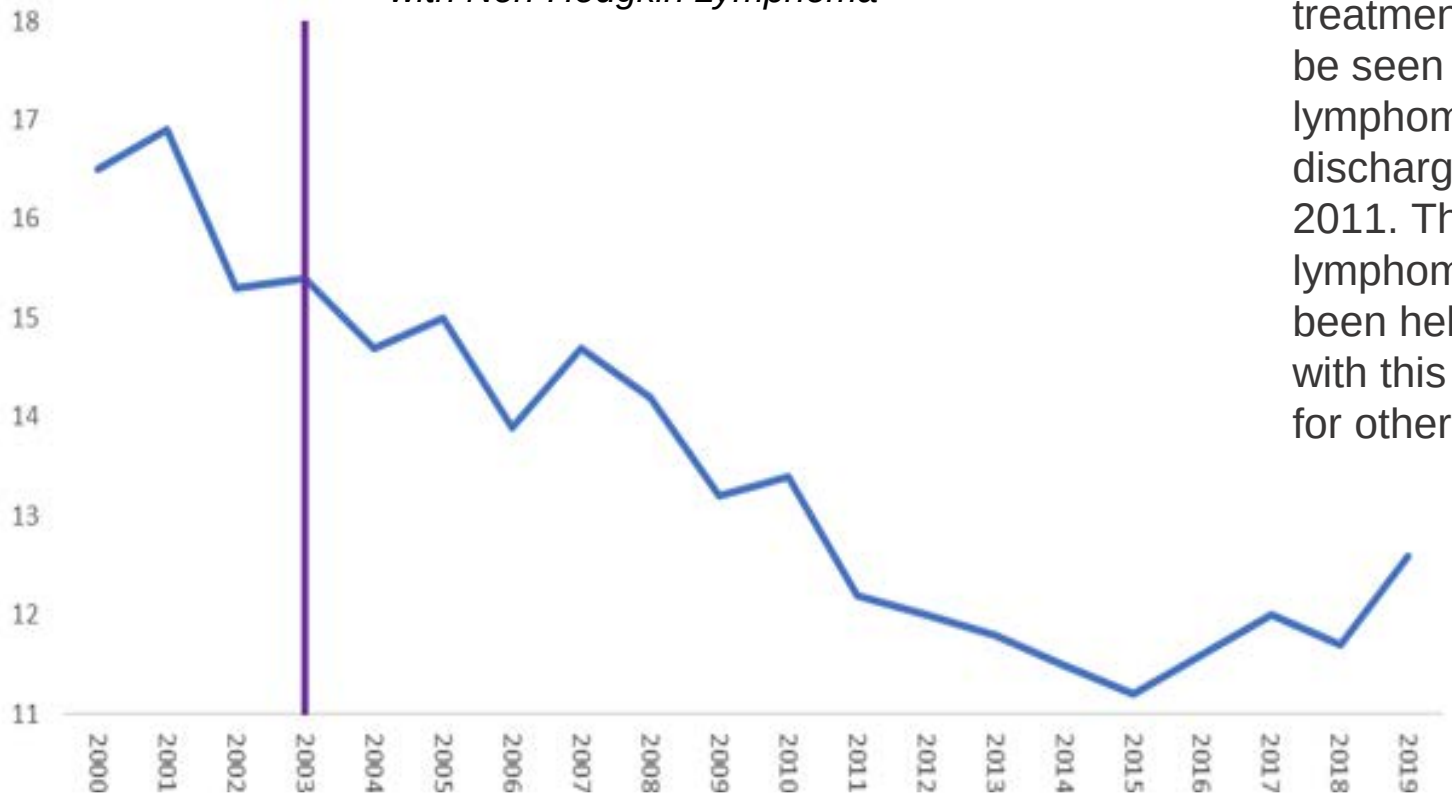
Disability bed days were defined as days in which a person was kept in bed for more than one-half of the day due to illness or injury.

Respondents with lymphoma had, on average, almost 4 fewer days of bed disability after 2003 compared with the period prior to 2003, declining from 18.5 days to 14.7 days per year. Adults without cancer and adults with any form of cancer had little to no change in bed days after 2003 compared to the period before 2003. These findings suggest that Velcade may have been responsible for a meaningful reduction in the annual number of bed days experienced by people with lymphoma.

Figure 32
H-3. Change in Healthcare Utilization for Conditions Addressed by New Vaccine or Therapy

Benefits from Velcade to Treat Multiple Myeloma and Mantle Cell Lymphoma—Healthcare Utilization

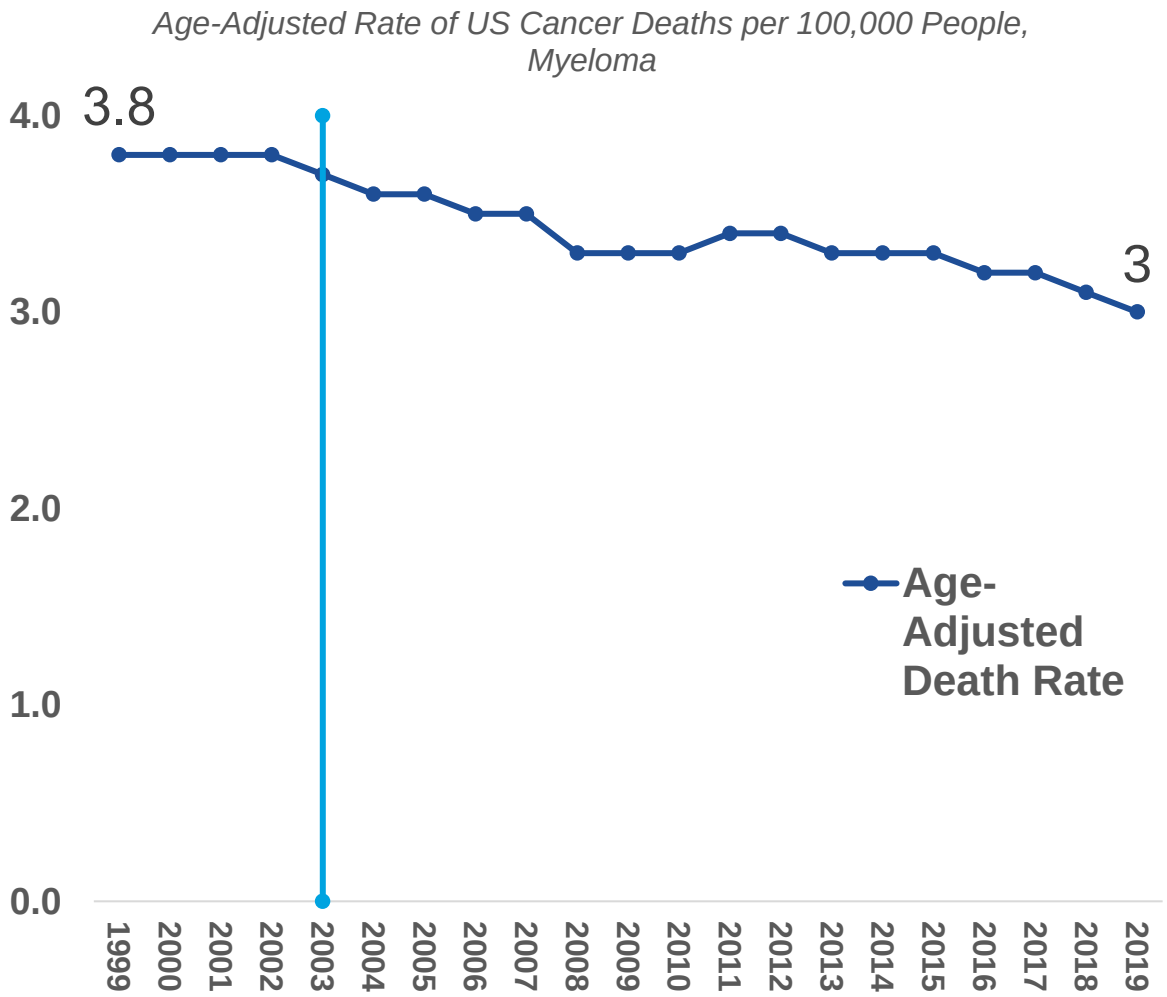
Hospitalization Discharge per 100,000 People with Non-Hodgkin Lymphoma



The inpatient discharge rate for non-Hodgkin lymphoma exceeded 16 per 100,000 in 2000 and 2001. The rate began decreasing in 2002, when Zevalin was approved for the treatment of non-Hodgkin lymphoma. Further declines can be seen after the 2003 approval of Velcade for mantle cell lymphoma, a type of non-Hodgkin lymphoma. Hospital discharge rates fell to approximately 12 per 100,000 by 2011. This promising trend in hospitalization utilization for lymphoma is suggestive that Velcade and Zevalin may have been helpful by reducing healthcare utilization for patients with this condition, preserving more capacity in the system for other patients.

Figure 33
H-5. Reduction in Mortality Due to New Therapies

Benefits from Velcade to Treat Multiple Myeloma and Mantle Cell Lymphoma—Mortality



The rate of death from myeloma has been decreasing. It is interesting to note that from 1999-2002, the rate of death from myeloma was stable at 3.8 deaths per 100,000 people.

However, 2003, the year Velcade was introduced, marked the beginning of a steady decline in death rates, from 3.8 per 100,000 people to 3.0 per 100,000 people in 2019. Although these findings do not account for overall trends in U.S. death rates, the reduction in myeloma deaths after 2003, following several years with no reduction in myeloma death rates, suggests that Velcade may have been at least partially responsible for the decline.

Impact of Gardasil for Prevention of HPV—Vaccination Coverage

Gardasil is a highly-effective vaccine that helps prevents human papilloma virus (HPV), the most common sexually transmitted infection in the U.S.[10] There are many different types of HPV, and some can lead to cervical cancer. The first HPV vaccine, Gardasil, received FDA approval in 2006 for female adolescents. Since then, several other HPV vaccines have been developed and used in the U.S. and globally, including Cervarix (FDA approval in 2009) and Gardasil 9 (2017).

In 2018, approximately 43 million HPV infections in the U.S. placed infected females at risk of future cervical cancer[10,11] Uptake of the HPV vaccine among adolescent females in the United States **increased from 37% of eligible females in 2008 (at least one dose) to 73% in 2019**. These coverage expansions are expected to reduce the cervical cancer burden below 2022 levels of 14,100 new cases and 4,280 deaths.[12]

Figure 34. HPV Vaccination Among Female Adolescents 2008-2019 in the United States

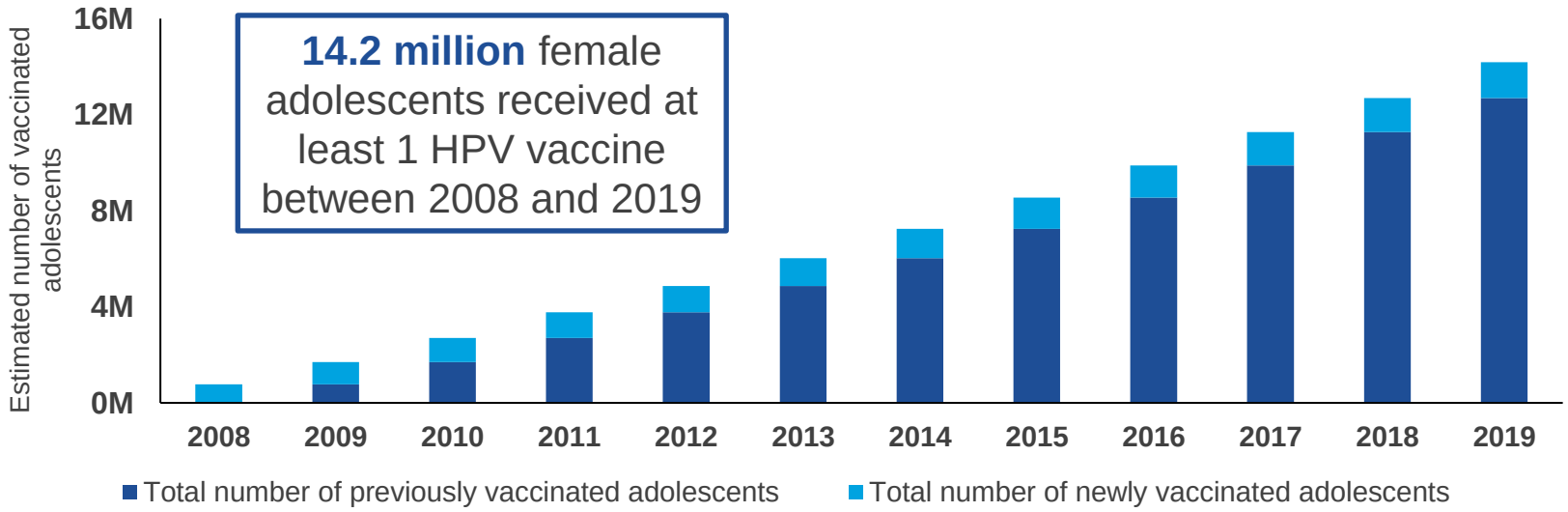
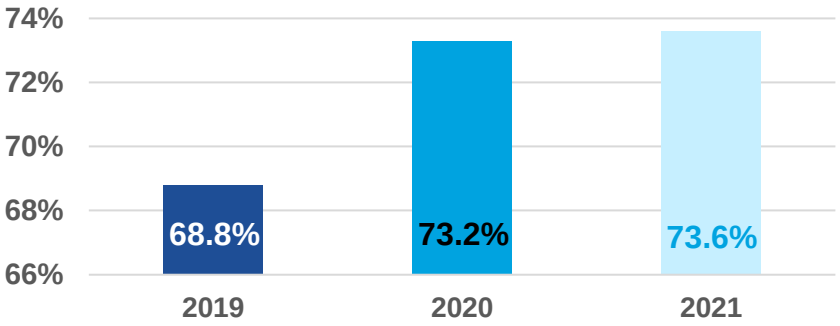


Figure 35. Average Global HPV Vaccination Coverage Among female Adolescents, 2019-2021*



HPV vaccine uptake in the U.S. is complemented by increased coverage of HPV vaccination globally. HPV vaccination is widespread in some countries, while other countries have relatively low coverage rates. Of the 54 countries reporting coverage rates for 2019-2021, the lowest coverage recorded was for Singapore (1% of eligible adolescent females) and the highest coverage was in Bhutan, Brazil, Ecuador, Mexico and Panama (99% of eligible adolescent females).

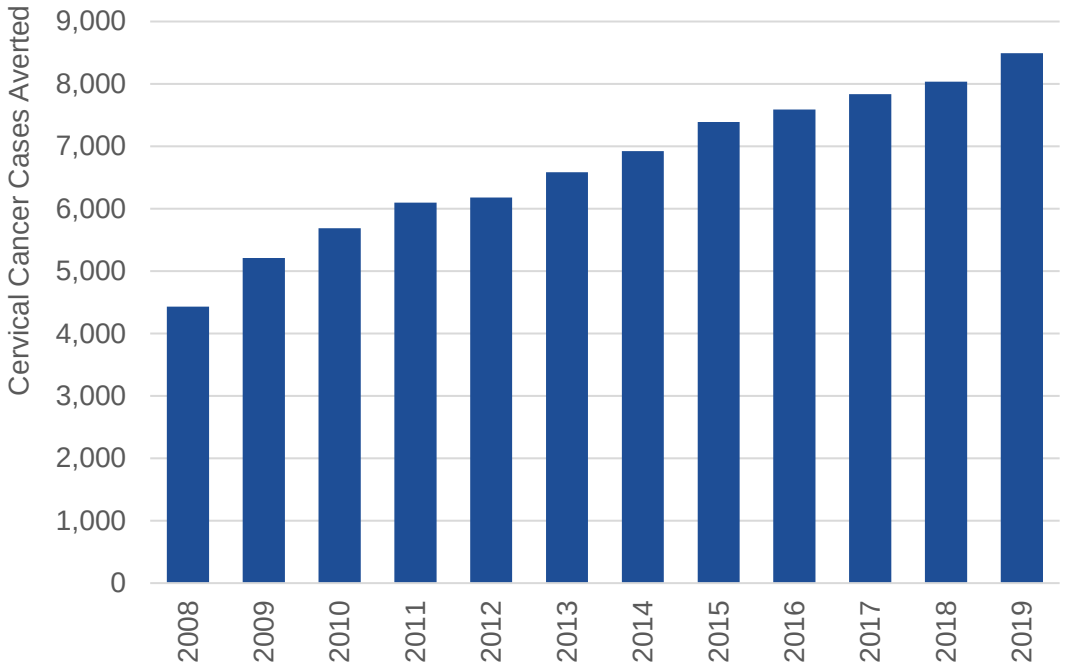
*Reflects sample size of 54 countries reporting coverage data over all three years

Figure 36
H-4. Reduction in Disease Incidence and Prevalence Due to Use of New Medical Products

Impact of Gardasil for Prevention of HPV—Disease burden

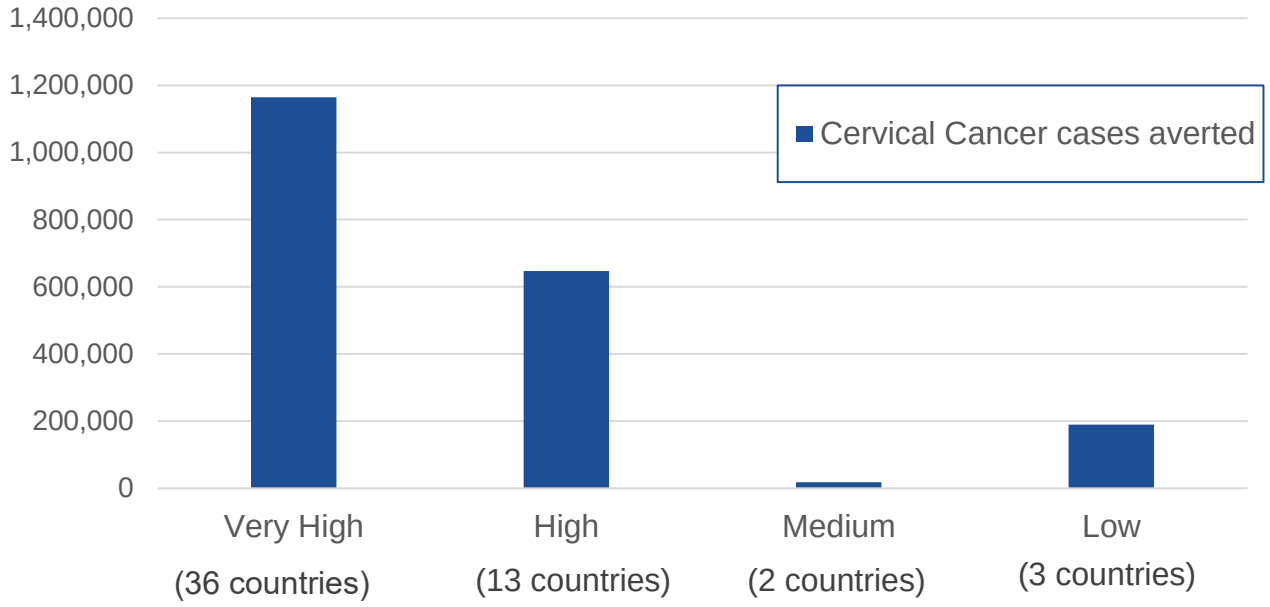
For the United States, we estimate that over 80,000 individuals would be likely to develop cervical cancer in the future if U.S. female adolescents had not been covered by at least 1 dose of Gardasil and other HPV vaccines between 2008 and 2019.

Figure 36. Estimated future cervical cancer cases averted in the U.S., 2008-2019



Globally*, an additional 2 million individuals would likely be diagnosed with cervical cancer in the future in the absence of Gardasil and other HPV vaccines. In the figure below, cases averted are shown for 4 levels of the Human Development Index (HDI), a composite measure of a country's life expectancy that is highly correlated with survival rates from cervical cancer.

Figure 36a. Cervical Cancer Cases Averted, 2019-2021



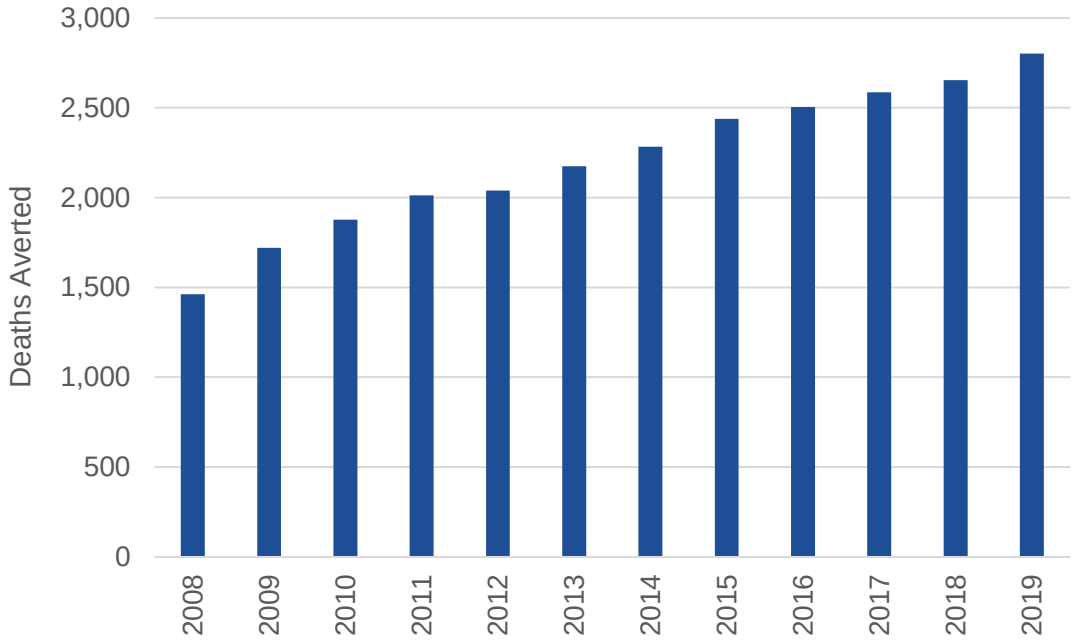
*Reflects sample size of 54 countries reporting complete coverage data from 2019-2021

Figure 37
H-5. Reduction in Mortality due to New Therapies (v2)

Impact of Gardasil for Prevention of HPV—Mortality

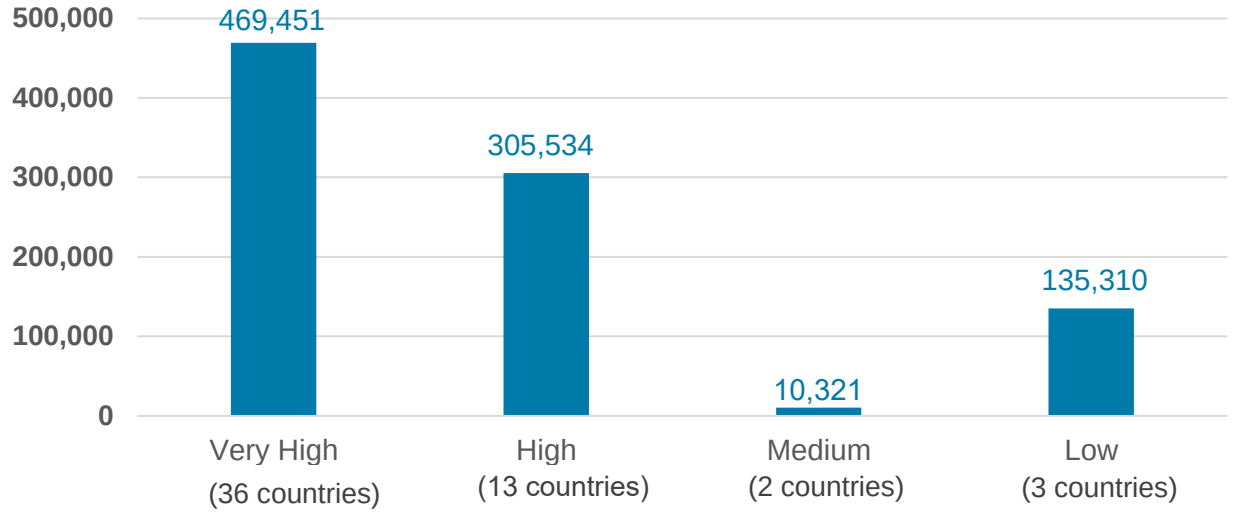
For the United States, we estimate that reducing the incidence of HPV as a result of HPV vaccination of female adolescents between 2008 and 2019 will avert over 26,500 future deaths from cervical cancer. **In aggregate, we estimate that 557,640 future years of life loss could be averted through HPV vaccination of females in the United States between 2008 and 2019.**

Figure 37. Cervical Cancer Deaths Averted in the U.S., 2008-2019



Globally, 921,000 future deaths from cervical cancer may be averted due to HPV vaccination.* In the figure below, deaths averted are shown for four levels of the Human Development Index (HDI), where death rates from cervical cancer vary from about 41% in very high HDI countries to 71% in low HDI countries. **In aggregate, we find over 18.4 million future years of life loss could be averted globally through HPV vaccination that occurred between 2019 and 2021.**

Figure 37a. Global Deaths Averted and Death Rate from Cervical Cancer, 2019-2021

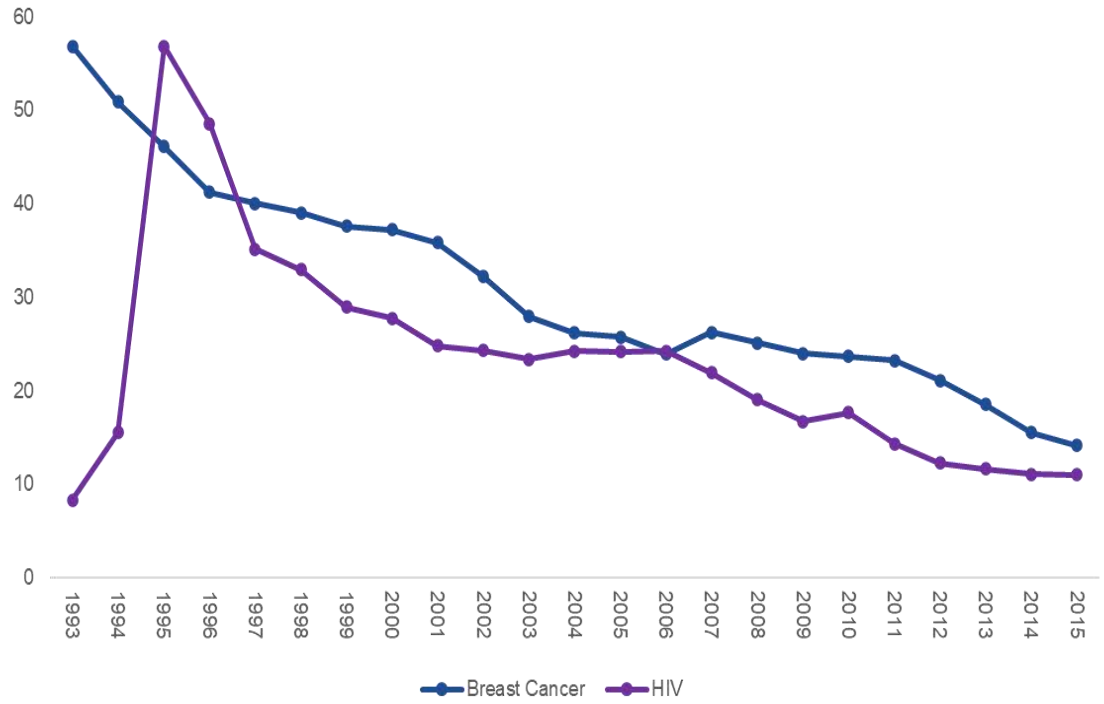


*Reflects sample size of 54 countries reporting complete coverage data from 2019-2021, incl. U.S.

Figure 38
H-3. Change in Healthcare Utilization for Conditions Addressed by New Vaccine or Therapy (v2)

Trends in Hospitalization Discharges for HIV Infection and Breast Cancer

Hospitalization per 100,000 People with Breast Cancer and HIV Infection



Hospitalization rates for HIV infection and breast cancer generally trended downward over the time periods following approval of products to treat these conditions. For example, 2 HIV products for HIV treatment were approved in 1991 and 1992, respectively, Videx and Hivid. After these approvals, hospitalization for HIV-related conditions initially increased to 57 per 100,000 population, possibly because of reductions in HIV deaths, then steadily decreased over time, falling to approximately 11 per 100,000 in 2015. Similarly, Taxol was approved to treat breast cancer in 1994, and breast cancer-related hospitalization rates continued their steady decline after that date, from more than 50 per 100,000 in 1994 to about 15 per 100,000 in 2015. These trends are suggestive that the products approved to treat HIV and breast cancer in the early 1990s may have been at least partially responsible for the declines in hospitalization discharge rates through 2015 for these conditions.

Notes: Data are from the HCUPnet. The diagnosis code of breast cancer is ICD-9-CM 174, and the diagnosis codes of HIV infection are ICD-9-CM 042, 043, and 044. It is worth noting that only first three quarters of discharge rates are available in 2015 due to the transition of diagnosis coding to ICD-10 codes.

5 Case Studies

Case Studies as an Impact Indicator

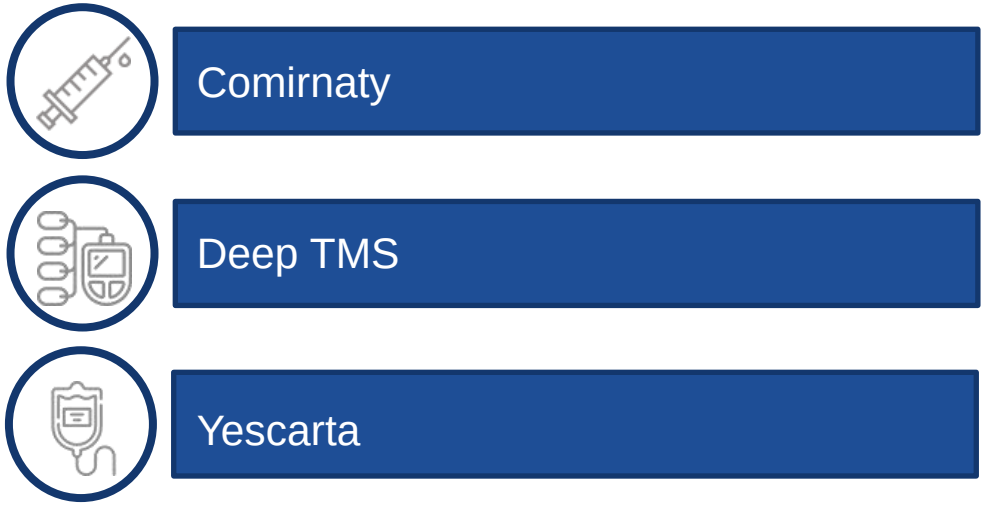
Quantitative impact indicators provide useful summary-level information that represents the aggregate impact of many activities over an extended period. However, these indicators must sacrifice specificity to present overall impacts and general trends. The technology transfer activities of the NIH IRP span a wide variety of technologies, partners, and products, as seen in the indicators presented in this document. A key feature of these technology licenses and their outputs and outcomes is that they also involve very complex processes. Since every license is negotiated separately, and the licenses frequently cover diverse combinations of IP, the process for achieving impact is not always consistent.

To help capture the details, complexities, and unique aspects of IRP technology licensing, four products were selected for qualitative case study analysis as listed in Figure 39. The three technologies represent key dimensions of overall impact:

- They represent the diversity of product categories involved in licensing, including pharmaceuticals, biologics, and devices.
- Certain cases (especially Comirnaty) achieved very broad adoption, as evidenced by their high sales volumes.
- The cases involved pioneering discoveries or inventions that led to extensive follow-on products or new technical approaches to treating diseases.
- The products did not have any adverse effects or other significant negative impacts.

Each case study will be presented in an abbreviated 1- or 2-page format (suitable as a handout or flyer for broad distribution), and a more detailed 4+-page format with additional discussion on the case's technical, legal, and business issues.

Figure 39. Products Based on NIH-Licensed Technologies Selected for Case Study Analysis



1-Page Case Studies

Figure 40 provides screen shots of 1-page version of the Comirnaty, Deep TMS, and Yescarta case studies. The case study research was informed by interviews with both the relevant NIH licensing officer and at least one of the inventors for each case. The analysis highlights the critical role that the technology transfer office played in enabling the commercialization of this significant innovation.

Comirnaty

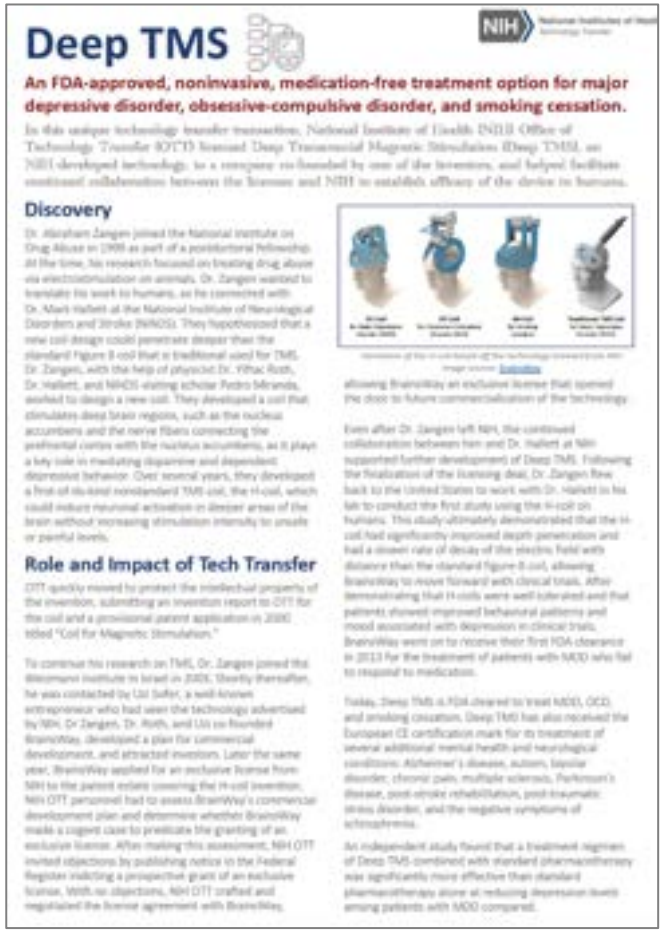
Pfizer-BioNTech's COVID-19 Vaccine

Discovery

Role and Impact of Tech Transfer

Comirnaty wouldn't be possible without the support of NIAID's Technology Transfer and Intellectual Property Office. They really had to work hard to bring it all together.

- Dr. Barney Graham

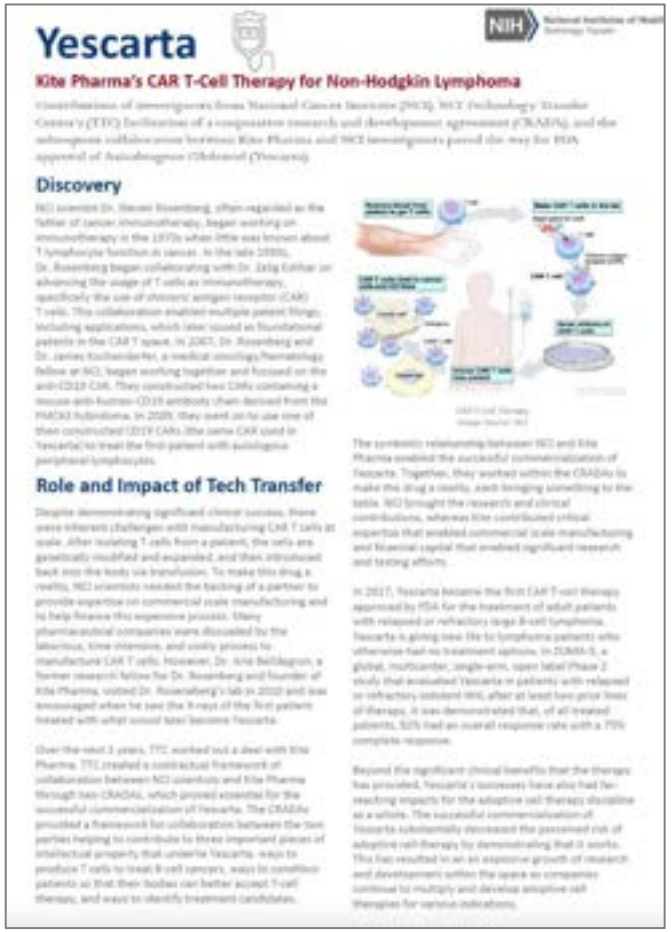


Deep TMS

An FDA-approved, noninvasive, medication-free treatment option for major depressive disorder, obsessive-compulsive disorder, and smoking cessation.

Discovery

Role and Impact of Tech Transfer



Yescarta

Kite Pharma's CAR T-Cell Therapy for Non-Hodgkin Lymphoma

Discovery

Role and Impact of Tech Transfer

Figure 40: 1-Page Case Studies

6 Notes and References

Notes

Section	No.	Note
1	1	Adapted from “About Science and Engineering Indicators” in National Science Board (2016), *Science and Engineering Indicators 2016*. Arlington, VA: National Science Foundation (NSB-2016-1).
	2	See Moyer, B. C., & Dunn, A. (2020). Measuring the Gross Domestic Product (GDP): The Ultimate Data Science Project. *Harvard Data Science Review,* 2(1). https://doi.org/10.1162/99608f92.414caadb
	3	Link, A.N., Siegel, D.S., & Van Fleet, D.D. (2011) Public science and public innovation: Assessing the relationship between patenting at U.S. National Laboratories and the Bayh-Dole Act, *Research Policy*, Volume 40, Issue 8, pp, 1094-1099.
	4	See http://www.patentsview.org
2	5	Vigene Biosciences. “Insect virus latest ally in gene therapy production,” *NatureResearch*. Available at https://www.nature.com/articles/d42473-018-00114-z
	6	According to the 2019 Business Enterprise Research and Development Survey, R&D spending as a share of sales is 16.6% for pharmaceutical firms, compared to 5.0% for all manufacturing firms and 10.9% for all firms in professional, scientific, and technical services. See Wolfe R; National Center for Science and Engineering Statistics (NCSES). 2021. *U.S. Businesses Reported Nearly a Half Trillion Dollars for R&D Performance in the United States During 2019, an 11.8% Increase from 2018*. InfoBrief NSF 22-303. Alexandria, VA: National Science Foundation. Available at http://ncses.nsf.gov/pubs/nsf22303
	7	“New drug and device approval in the United States take an average of 12 and 7 years, respectively, from pre-clinical testing to approval.” See Van Norman, Gail (2016). “Drugs, Devices, and the FDA: Part 1: An Overview of Approval Processes for Drugs,” *JACC: Basic to Translational Science*. 2016 Apr 25;1(3):170-179.
3	8	Pressman, L., Planting, M., Yuskavage, R., Bond, J., and Moylan, C. (2018*) A Preliminary Application of an I-O Economic Impact Model to US Federal Laboratory Inventions: 2008-2015.* Report prepared for the National Institute of Standards and Technology, July.
	9	French, T. (2018, June 7). Interpreting Employment Impacts. IMPLAN. https://blog.implan.com/interpreting-employment-impacts.
4	10	Centers for Disease Control and Prevention. (April 12, 2022). Human Papilloma Virus (HPV) – HPV Fact Sheet. Accessed October 19, 2022. https://www.cdc.gov/std/hpv/stdfact-hpv.htm
	11	Centers for Disease Control and Prevention. (2021). Cancers Associated with Human Papillomavirus, United States—2014–2018. USCS Data Brief, no. 26. Accessed October 19, 2022. https://www.cdc.gov/cancer/uscs/about/data-briefs/no26-hpv-assoc-cancers-UnitedStates-2014-2018.htm
	12	National Cancer Institute. SEER Cancer Stat Facts: Cervical Cancer. (n.d.). Accessed September 14, 2022. https://seer.cancer.gov/statfacts/html/cervix.html