



# Public Support for Late-Stage New Drug Discovery

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**Scholarly Report submitted in partial fulfillment of the MD Degree at  
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**Scholarly Report Title:** Public support for late-stage new drug discovery

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## Abstract

**Title:** Public support for late-stage new drug discovery

**Rahul K Nayak, Jerry Avorn, Aaron S. Kesselheim**

**Purpose:** To determine the role of publicly-supported research in the development of innovative new medications.

**Method:** We examined patent data and drug discovery and development histories to assess the extent of public support for late-stage medication development for all new drugs approved by the US Food and Drug Administration (FDA) containing one or more new molecular entity approved between January 2008 and December 2017 via the new drug application pathway. We looked for evidence of patents or drug development history documenting late-stage research contributions by publicly funding to an academic center or closely related a spin-off company, as well as each drug's approval pathway and first-in-class designation.

**Results:** Over the 10-year study period, the FDA approved 248 novel drugs containing one or more new molecular entities. We found that 62 (25%) of these drugs were based at least in part on patents or other late-stage intellectual contributions by publicly-supported research. Of these, 48 drugs (19%) had origins in publicly-supported research and development and 14 (6%) originated in in companies spun-off from a publicly-supported research program. Drugs with public-sector provenance were more likely to receive an expediated FDA approval or be designated first-in-class, indicating their relative therapeutic importance.

**Conclusions:** A review of the patents associated with new drugs approved over the last decade indicates that publicly-supported research played a major role in the development of a substantial proportion of new medications, either through direct funding of late-stage research or the creation of resultant spin-off companies. This may have implications for policy makers in determining fair prices and revenue flows for these products.

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## **Glossary of Abbreviations**

FDA – Food and Drug Administration

FOIA – Freedom of Information Act

NDA – New Drug Application

NIH – National Institutes of Health

NME – New Molecular Entity

Orange Book - Approved Drug Products with Therapeutic Equivalence Evaluations

## Scholarly Contribution

This project examined the contributions of publicly-funded research in late stage research for new drugs approved by the US FDA between 2008 and 2017. The traditional view of the biomedical research enterprise is that publicly-funded research (including research conducted in government labs, academic institutions, or through philanthropic non-profit research institutions) supports upstream, basic science research and that the pharmaceutical industry supports the late-stage research (i.e., research resulting in patents on the drug product or other key intellectual contributions to the drug's development) leading to the invention of a new drug as well as its support for its development through clinical trials. However, older studies have found an increasing share of drugs in which publicly-funded research contributes to this late stage research, but no data exists for drugs approved over the last 10 years. We aimed to clarify the role of publicly-funded research for drugs approved over the last 10 years. Public-sector institutions that hold patents on drugs or ownership stake in spin-off companies may have a greater than appreciated role in drug prices due to economic leverage during the technology transfer process. In addition, the government retains several rights on government-funded inventions (i.e., "march-in-rights"). With increasing attention on high pharmaceutical prices, this research helps better characterize the biomedical research enterprise and potential policy interventions given the contemporary discussion on high drug prices.

**Contributions:** RKN contributed to design, collection of data, analysis, conduct, statistical analysis, interpretation of results, and primary draft of manuscript; JA contributed to design, interpretation of results, and revision of manuscript; ASK contributed to the design, interpretation of results., and revision of manuscript. All authors contributed to and approved the final manuscript.

**Appendix: Submitted Manuscript**  
**Public support for late-stage new drug discovery**  
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The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

## **Summary Box**

### **What is already known on this topic**

- Publicly-sponsored research plays a substantial role in the upstream, basic science investigations behind most new drugs.
- The role of publicly-sponsored research in late-stage research leading to drug discovery is more controversial.
- Prior studies have also shown that 13.6% of new molecular entities approved between 1990-2007 had their origins in publicly-sponsored research.

### **What this study adds**

- This study examines all new small molecule drugs approved by the FDA between January 2008 and December 2017 containing a new molecular entity.
- A quarter (25%) of recently approved drugs had key late-stage research contributions from publicly-sponsored research institutions (19%) or resultant spin-off companies (6%), often with key patents on the drug owned by these institutions. These drugs were more likely to receive an expediated approval and be a first-in-class drug, suggestive of their relative therapeutic importance.
- Publicly-sponsored research has a greater role in drug discovery than previously appreciated. This may have policy implications for debates on drug pricing.



## **Abstract**

**Objective:** To determine the role of publicly-supported research in the development of innovative new medications.

**Design:** We examined patent data and drug discovery and development histories to assess the extent of public support for late-stage medication development.

**Setting:** All new drugs approved containing one or more new molecular entity approved by the US Food and Drug Administration (FDA) between January 2008 and December 2017 via the new drug application pathway.

**Main outcome measures:** Patents or drug development history documenting late-stage research contributions by publicly funding to an academic center or closely related a spin-off company, as well as each drug's approval pathway and first-in-class designation.

**Results:** Over the 10-year study period, the FDA approved 248 novel drugs containing one or more new molecular entities. We found that 62 (25%) of these drugs were based at least in part on patents or other late-stage intellectual contributions by publicly-supported research. 48 drugs (19%) had origins in publicly-supported research and development and 14 (6%) originated in in companies spun-off from a publicly-supported research program. Drugs with public-sector provenance were more likely to receive an expediated FDA approval or be designated first-in-class, indicating their relative therapeutic importance.

**Conclusions:** A review of the patents associated with new drugs approved over the last decade indicates that publicly-supported research played a major role in the development of a substantial proportion of new medications, either through direct funding of late-stage research or the creation of resultant spin-off companies. This may have implications for policy makers in determining fair prices and revenue flows for these products.

Publicly-supported research funds much biomedical research conducted at universities, academic medical centers, other non-profit organizations, and government laboratories. In the US, such support comes primarily from the National Institutes of Health (NIH), but also from other federal or state entities, disease-focused charities (e.g., the Cystic Fibrosis Foundation), or biomedical research philanthropies (e.g., the Howard Hughes Medical Institute). Such research often plays a key role in elucidating potential drug targets and understanding the pathophysiology of disease — activities that are central to drug discovery. This upstream research may stretch back several decades before a drug reaches clinical trials or is approved by the US Food and Drug Administration (FDA) or another regulator.<sup>1</sup> One recent report found that NIH funding contributed to published research associated with all 210 new drugs approved by the FDA from 2010-2016.<sup>2</sup> In addition, public support often covers the costs of later-stage translational research, and may even cover the conduct of some clinical trials. At some point in the development cycle of most prescription drugs, pharmaceutical manufacturers become involved and expend substantial resources in final drug development, moving drugs through pivotal clinical trials and FDA approval, and developing means of large-scale production. For some medications, their discovery and development occur largely within the corporate sector, but this is uncommon.

The role of public-sector contributions versus those of the pharmaceutical industry to new drug discovery remains controversial, with some arguing that companies' investment in drug discovery is the key source for new drug development.<sup>3</sup> This view, along with the costs of conducting clinical trials, is used to justify high drug prices,<sup>4-6</sup> although the actual cost of drug development is hard to accurately estimate.<sup>7</sup> The relative contributions of publicly-supported research and the pharmaceutical industry can be difficult to separate for particular product. However, it is generally agreed that the upstream basic science research on which so many new drugs depend is predominantly funded by public support, while clinical trials are predominantly funded by the pharmaceutical industry.

One key issue in the drug development continuum is which research justifies patent claims on the drug – the basis of drug ownership and pricing. Such patent generating research tends to occur at a later point in the continuum, because patent law requires

inventors to describe a well-defined product or process before a patent can be issued. Other patentable steps can cover a drug's synthesis, the chemical composition of its active ingredient, or its method of use. These patents provide the basis for post-approval market exclusivity, granting the patent-holder ownership over the product and therefore the capacity to control the drug's US price. In other markets, patent-based levers have been used to achieve public policy goals, such as helping to ensure access to essential drugs in low-income settings around the world.<sup>8-12</sup>

Prior studies have reviewed the data submitted to the FDA to investigate to what extent public-sector research support that contributes to drug development is reflected in these patents. While it's well known that there are often many follow-on patents not germane to a drug's underlying innovation associated with a drug, the patents submitted to the FDA Orange Book are typically those considered key to the drug's invention and clinical use. These studies found public-sector research institutions to be the sources of 4.6% of new molecular entities (NMEs) approved 1981-1990,<sup>13</sup> 6.7% of new drugs approved 1990-1999,<sup>4</sup> 10.3% of NMEs approved 1988-2005,<sup>14</sup> and, most recently, 13.6% of NMEs approved between 1990-2007.<sup>15</sup> Increasing proportions of publicly-supported research contributions have been attributable to a changing research and development landscape.<sup>15</sup>

Public-sector research support has continued in the last few decades—although until recently had fallen in inflation-adjusted terms—while some large pharmaceutical manufacturers have closed laboratories and focused on purchasing drugs developed in start-up companies, many spun out of public-sector research institutions. We therefore sought to examine whether there has been a change in the way publicly-supported research for new FDA-approved drugs containing an NME is reflected in patent data between 2008-2017, and specifically whether there has been a role for startup biotechnology companies emerging from publicly-supported research.

## **Methods**

### Data Collection

#### *Drug Approval*

We identified all new drugs approved between 2008 and 2017 using the Drugs@FDA database,<sup>16</sup> including all drugs approved through the new drug application

process for small (non-biologic) molecular entities. Biologic therapies, vaccines, and gene therapies were excluded as they are approved through a separate biologic license application pathway for which patent information is not collected by the FDA. Novel drugs were identified based on the FDA's Type 1 approval designation and FDA lists of NME approvals by year.<sup>1</sup> Therapeutic categorization was assigned based on the drug's initial FDA-approved indication.

### *Approval Pathway*

We defined the characteristics of a drug's approval pathway using FDA published designations of drugs that received standard, priority, accelerated, breakthrough, fast track, first-in-class, and/or Orphan Drug Act designation; a drug may have received more than one of these. We considered the designation only for a drug's initial approval. In several years (2008-2010), the FDA did not publish fast track designation or classify drugs as first in class on their website. For those years, we used prior work to define drugs which received fast track designation and first-in-class designation.<sup>17,18</sup> A full list of all drugs studied and their FDA approval pathways is included in the supplementary table (Table S1).

### *Patents*

We then obtained patent data for each approved drug from several sources. We issued a Freedom of Information Act (FOIA) request to obtain historical Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book") datafiles for 2001-2017, which along with a data file from March 2018, were used to obtain patent data submitted to the FDA, including those that may be presently expired. The FDA requests that all key patents for a given drug be submitted by its manufacturer for inclusion in the Orange Book. This include patents on the drug's substance, product, or method of use. The Merck Index, a chemical entity reference, was used to supplement patent information and typically listed one or two key patents related to the drug's synthesis or final formulation.<sup>19</sup>

We next obtained data from patent applications for the study drugs by using the PatentsView Application Program Interface developed by the United States Patent and Trademark Office and the PatentsView R package, using the programming language R

version 3.5.0.<sup>20,21</sup> This allowed identification of a patent’s inventor and the organization assigned ownership. We manually investigated patents that could not be queried using this method to determine the inventor and assigned ownership for each product.

### *Patent Assignee Analysis*

To characterize the development pathway for each drug, we examined the assignee information for each patent and conducted web searches to classify the organization as either a publicly-supported institution (universities, hospitals, non-profit foundations or institutions, or government laboratories) or a private, non-public organization (primarily biotechnology or pharmaceutical companies). Whenever possible, we identified start-up firms spun off from publicly-supported research institutions.

### *Drug Monographs*

Examining only the patent information from the FDA Orange Book and the Merck Index could provide an incomplete understanding of the key intellectual contributions to a drug’s invention. For example, this approach could miss patents that expired prior to drug approval or when patents were intentionally not pursued. We therefore supplemented these patent analyses with a drug monograph database, AdisInsight, that characterizes a drug’s research and development history and assigns the “originators” and “developers” for each drug.

### *Drug Development Histories*

We examined available publications regarding the drug’s development history (e.g., Nature Reviews Drug Discovery), Wikipedia entries, researcher/inventor biography pages, news articles, and academic technology transfer pages. Through a similar approach we also independently verified entries from AdisInsight to determine whether there was evidence of key intellectual contributions from publicly-supported research.

## Data Analysis

### *Determining Public-sector Contributions*

We considered a drug to have a late-stage research contribution from publicly-supported research if we found any patents for the product that were owned by a publicly-

supported research institution or that declared government funding (i.e., a “government interest” statement). We also included drugs listed in the drug monograph database as originating in a publicly-supported research institution and which had compatible histories. Lastly, for several drugs we discovered contributions by publicly-supported research through review of drug development histories. For combination drugs that contained one new molecular entity (e.g., anti-viral therapies), we considered the drug to have contributions from publicly-supported research if one or more of the active ingredients had contributions from a publicly-supported research .<sup>15</sup>

Finally, we examined the private companies that held patents on a drug or were deemed to be an “originator” by AdisInsight, to determine if the company had been spun off from a publicly-supported research institution. If we found evidence that a drug was based on the same technology or innovation that initially resulted in the creation of a spin-off company, we classified it as having a late-stage contribution from a publicly-supported research spin-off. We excluded drugs unrelated to a company’s original spin-off product or technology.

Many aspects of a drug can be patented, with some representing more important innovation than others. To address this, we employed three approaches. First, for each drug we calculated the share of patents held by publicly-supported research institutions and their spin-offs. Second, we determined whether the first patent was held by a publicly-supported research institution or a spin-off. Third, we examined Orange Book patents to see if publicly-supported research led to patents on the drug’s ‘substance’ or ‘product,’ (as opposed to methods of use) which are typically more foundational.

## **Results**

### Patent and Originator Information

We identified 248 novel drugs containing a NME approved for the first time between January 2008 and December 2017 (21 were combinations, some of which had more than one NME, leading to 253 NMEs). Using the Orange Book, we identified at least one patent for 229 (92%) products. The Merck Index identified at least one patent for an additional 14 (6%) products, leaving five products (2%) with no available patent

information. We identified drug monographs for 246 (99%) products, and patent or monograph data were available for 247, representing all but one drug.

### Publicly-supported Research Contributions

Our review of patents and supporting data found that one-quarter (62) of all new products had late-stage research contributions from a publicly-supported research institution or closely related spin-off company. The drug classes most likely to be connected to publicly-supported research or spin-off patents were largely concordant with the overall number of approvals by drug class (Table S2).

Forty-eight products (19% of the all new drug approvals) had evidence of direct publicly-supported research. For all but one, the contributions were related to the drug's discovery, synthesis, other key intellectual property (Table 1).<sup>22</sup> For 30 medications, publicly-supported research institutions directly held one or more patents. Another 8 drugs had direct publicly-supported research origins, though the patents found were held by the corresponding spin-off company. The remainder of drugs with public-support contributions were found through the drug monograph database and investigations of the drugs' discovery and development histories. One of these drugs, benznidazole, a treatment for Chagas disease, is a unique case as it received development support by the Drugs for Neglected Diseases Initiative and others for FDA approval and is being sold on a "no profit no loss basis."<sup>22</sup> However, it was originally developed by Hoffman-La Roche in the 1970s, who then donated the rights to the drug to the Brazilian government in 2003.<sup>23</sup>

Fourteen (6%) drugs were developed by companies that were spun-off wholly or in part on publicly-supported research; all but two were identified through patents listed in the Orange Book (Table 2). For example, the hepatitis C treatment sofosbuvir (Sovaldi) and other sofosbuvir-containing combination drugs were in this category as they originated at Pharmasset, a spin-off company based on federally funded research performed at Emory University.<sup>24</sup> In addition to these 14 drugs, we found at least ten other drugs that had origins in spin-off companies, but these were excluded as it was unclear if these drugs were related to the technologies or drugs that initially gave rise to the spin-off company.

### Patent Characteristics

Of the 48 drugs identified as having late-stage publicly-supported research contributions, 38 (80%) had at least one patent held by a publicly-supported research institution or spin-off company. For these drugs, 70% (95% confidence interval [CI]: 60-81%) of the patents, on average, were held by a publicly-supported research institution or spin-off (Table 3). A US government interest statement was declared on at least one patent for 17 drugs. For 32 (84%) drugs, the first patent identified was held by a publicly-supported research institution or spin-off. Thirty-five drugs had Orange Book patents related to the drug's substance, product, or method of use. Of these, publicly-supported research institutions or spin-offs held at least one patent on either the drug's product or substance for 27 (77%) drugs, representing foundational patents on the drug. Similar findings were noted for drugs with late-stage contributions from a spin-off company (Table 3).

#### FDA Approval Process

New drugs based on contributions from publicly-supported research or spin-off companies were more likely to receive FDA approval through one or more expedited development or review pathways than new drugs without these characteristics (68% vs. 47%,  $p = 0.005$ ) and to be first in class (45% vs 26%,  $p = 0.007$ ; Table 4).

#### **Discussion**

We studied all new drugs approved by the US FDA from 2008-2017 to determine whether their patents or other late-stage drug discovery contributions documented origins in publicly-supported research.

The development of a new medication is a complicated process. Important and costly contributions often come from both the public and private sectors, in varying proportions. Under current patent law, making a seminal discovery about an important drug target, or even taking development of a new approach almost to the point of creating a marketable product, are not sufficient to win intellectual property rights over the medication that emerges from this chain of research. While substantial private investments were critical for many medications for intellectual contributions, funding the clinical trials, and regulatory compliance necessary to win FDA approval, the role of the publicly-



supported research investments which served as the basis of the drug's discovery are often not as clearly attributed.

Our analysis found that publicly-supported research (19%) or spin-off companies that had origins in public funding (6%) made important late-stage intellectual contributions to one in four new drugs approved in the last decade. These data highlight the substantial and increasing role of late-stage publicly-supported research leading to new medications, in addition to the more widely acknowledged contributions of public funding to the foundational basic science discoveries on which most new products are based.

This study has several limitations. First, we did not attempt to weigh the relative importance of public- versus private-sector innovation for particular drugs, and acknowledge that for many products important private (corporate) investment occurred along with public sector funding. As a result, we are not concluding that the substantial contributions of public support to late-stage drug development would confer partial public ownership of those products under current patent law. In fact, the flow of publicly-funded research knowledge into the private sector for commercialization appears to have been a major goal of the original Bayh-Dole legislation, rather than an "adverse effect" of it.<sup>25</sup>

In this analysis, we identified a product as having a late-stage publicly-supported research component if the patent and drug-discovery history documented a key contribution by such entities in its development. This does not mean that such public investment was the only source of a drug's creation, or that there was no private-sector contribution as well. Second, our analysis relies primarily on patents listed in the FDA Orange Book and proprietary databases of drug development to identify public-sector origins, which represents a limited set of patents associated with a drug. Further investigation into the origins of each drug might have yielded additional relevant information. In addition, we may be undercounting the contributions of publicly-supported academically-based researchers who collaborate with pharmaceutical companies, for example, if patent derived from such collaboration are held by the sponsor. Third, a major limitation is that we did not include biologic agents in this study despite their clinical and economic importance. This was because the FDA does not collect patent data for drugs approved through the biologic license application process. Biologics are increasing share of all approved drugs and they represent a critical class of specialty pharmaceuticals that are

often quite expensive; moreover, the current regulatory framework limits the opportunity to produce generics. Further research to investigate the role of late-stage publicly-supported research for biologics is necessary. Lastly, we limited our investigations to English language publications, websites, and media coverage to verify key contributions made by publicly-supported research.

Our patent-based approach will underestimate the additional role of upstream basic and translational science research supported by public funds that is critical to the discovery of new drugs; this contribution has been clearly described by others.<sup>2,26</sup> We also did not tabulate the cost of clinical development within industry required for final product development and regulatory approval, which can be substantial.

One difference between our analysis and prior studies is that earlier research relied predominantly on patent data submitted to the FDA Orange Book,<sup>4,13-15</sup> which may underestimate the role of publicly-supported research if patents had expired at the time of drug approval, were never pursued, or were held by spin-off companies. Limiting our analysis to only those drugs with patents held by publicly-supported research institutions would have identified 30 drugs, or just 12% of new approvals. Incorporating other patent sources, drug histories, and basic investigations to confirm a drug's development history, including the role of spin-off companies with origins in publicly-supported research, more accurately represents the late-stage contributions of public-sector funding to drug discovery and development.

These findings also reflect the continuing trend of an increased role of publicly-supported research in late-stage research leading to new drug discovery, that was also seen in previous studies.<sup>4,13-15</sup> This may be because of ongoing Congressional funding of biomedical research through the NIH since the 1990s.<sup>27,28</sup> The fruits of that earlier publicly-supported research would be seen in recent drug approvals, as it typically takes a decade or more from drug discovery to approval. In addition, university-owned patents have increased as a share of all US patents from 0.28% in 1969 to 0.83% in 1985 to 1.89% in 2012,<sup>29</sup> reflecting increased productivity as a result of more biomedical research funding as well as policies to more actively pursue patents by maturing technology transfer offices in the nearly four decades since passage of the Bayh-Dole Act.<sup>30</sup> For example, we identified at least 17 drugs products for which US government interest was disclosed on patents; this

likely is an underestimate as there is evidence that government funding is under-disclosed on patent applications.<sup>9,31,32</sup>

Our data also indicate that drugs with publicly-supported research or spin-off contributions are 1.4 times as likely to receive an expedited FDA approval process and 1.7 times as likely to be first-in-class. While these are crude measures of innovativeness, this suggests that publicly-supported research is not only leading to new drugs but also new classes of drugs with novel mechanisms of action – a finding consistent with prior studies.<sup>15,28,33-35</sup>

These findings have several implications for health care and regulatory policy, particularly in the US. The total US biomedical enterprise has been responsible for making possible a substantial proportion of new drug development,<sup>36</sup> though by no means all of it.<sup>37</sup> At the same time, drug prices are substantially higher in the US than anywhere else in the world, with Americans paying on average about twice the per-capita amount for prescription drugs as citizens of other advanced industrialized countries.<sup>38,39</sup> Identifying drugs with late-stage publicly-supported research contributions, particularly those for which such institutions hold key patents, could represent a potentially useful policy lever. Such drugs include nusinersen (Spinraza, for spinal muscular atrophy; list price: \$750,000 in the first year),<sup>40</sup> eliglustat (Cerdelga, for Gaucher disease; \$310,250/year),<sup>41</sup> and enzalutamide (Xtandi, for prostate cancer; \$129,000/year).<sup>42</sup> The prices of these drugs, each of which was based on very substantial academic development, have been criticized in the US and all are substantially lower priced in other countries. For these and other drugs, the contributions of publicly-funded research to their development could be expected to be compensated by more favorable licensing and royalty arrangements by the product's manufacturer to the non-profit entities that played such a large role in their discovery and development. Some have questioned whether such payments represent adequate compensation to the innovator institution for its role in drug development.<sup>43</sup> Additional issues arise concerning the fairness of high prices in the many instances in which the public already made investments a drug's creation, such as through taxpayer support of NIH funding.<sup>44,45</sup> At a time when rising drug prices are defended as being necessary to fund industry innovation, without which new treatments would be expected to slow dramatically, our findings can inform this public discussion.

In theory, the federal government retains a fully paid-up license, as well as “march-in rights,” for patents with government-funded origins. These rights could allow the government to use the patented product for its own purposes or, in the case of march-in rights, grant additional licenses to others if needed to address health needs. However, to our knowledge, neither right has ever been used by a federal agency for pharmaceutical products, even in the face of critical drug shortages or extreme price spikes.<sup>8</sup> In addition, hundreds of public-sector institutions have recognized their obligation to make technology transfer agreements that will promote the public’s interest and equitable access to medicines.<sup>10-12</sup> While these technology transfer principles were developed and implemented primarily to promote access in low- and middle-income countries, this approach could also be used to ensure the US public has access to taxpayer-funded inventions.

## **Conclusion**

We reviewed comprehensive patent and related data to trace the contributions of publicly funded research to the late-stage development of new medications. Our findings highlight the important role played by public and philanthropic funding in the drug research and development ecosystem. We found that such institutions and the corporate spin-offs they made possible were central to the development of at least a quarter of all new drugs approved by the FDA between 2008-2017, either through direct contributions to drug development (19% of new drugs) or through the formation of spin-off companies based on earlier public funding (6% of drugs). Medications approved following major public sector funding were more likely to receive an expedited development or approval pathway designation from the FDA and more likely to be a first in class therapy, suggesting that they were more likely to be novel and potentially clinically important.

Our findings also document a substantial increase in the share of drugs with publicly-supported research origins compared to prior studies, likely reflecting our more comprehensive methodologic approach, growing taxpayer funding for biomedical research, and increased pursuit of patents by public-supported research institutions over the last several decades. These findings provide additional data for the ongoing debate on support for public-sector biomedical research, and the best ways to take these key contributions

into account in determining the ownership of and fair prices for new drugs, especially those priced at extremely high levels.

**Table 1: New drugs with publicly-supported research contributions**

App. Date	App No.	Drug Name (Generic)	Manufacturer	Institution	US Government Contribution*	Source used to determine drug origin
3/20/2008	#022249	BENDAMUSTINE HYDROCHLORIDE	CEPHALON	Institute for Microbiology and Experimental Therapy (German Democratic Republic)		Drug History
4/24/2008	#021964	METHYLNALTREXONE BROMIDE	SALIX PHARMS	University of Chicago (PHS/HHS)	Yes	Patent
7/3/2008	#022090	GADOXETATE DISODIUM	BAYER HEALTHCARE	Massachusetts General Hospital		AdisInsight
9/19/2008	#022290	IOBENGUANE SULFATE I-123	GE HEALTHCARE	University of Michigan	Yes	Patent (Merck Index)
10/28/2008	#022253	LACOSAMIDE	UCB INC	University of Houston / Research Corporation Technologies (NIH)	Yes	Patent, AdisInsight
12/15/2008	#022311	PLERIXAFOR	GENZYME	Rega Institute for Medical Research		AdisInsight
12/22/2008	#021711	GADOFOSVESET TRISODIUM	LANTHEUS MEDCL	Massachusetts General Hospital		Patent, AdisInsight
4/7/2009	#022268	ARTEMETHER; LUMEFANTRINE**	NOVARTIS	Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences (China)	Yes	Patent
9/24/2009	#022468	PRALATREXATE	ALLOS	Sloan-Kettering Institute for Cancer Research, SRI International, Southern Research Institute (NCI)	Yes	Patent
11/5/2009	#022393	ROMIDEPSIN	CELGENE	Harvard University/University of Tokyo		Drug History

11/16/2009	#022395	CAPSAICIN	ACORDA	University of California		Patent
1/22/2010	#022250	DALFAMPRIDINE	ACORDA	Purdue University		Drug History (Technology Transfer Website)
8/13/2010	#022474	ULIPRISTAL ACETATE	LAB HRA PHARMA	US Department of Health and Human Services/Army/NIH /National Institute of Child Health and Human Development	Yes	Patent
11/15/2010	#201532	ERIBULIN MESYLATE	EISAI INC	Harvard University/NCI	Yes (no patent)	AdisInsight
4/28/2011	#202379	ABIRATERONE ACETATE	JANSSEN BIOTECH	The Institute of Cancer Research (UK)/ University of London		Patent, AdisInsight
5/2/2011	#201280	LINAGLIPTIN	BOEHRINGER INGELHEIM	University of Toronto, Tufts, New England Medical Center Hospitals	Yes	Patent
10/14/2011	#021825	DEFERIPRONE	AOPHARMA INC	University of Toronto / Royal Free and University College Medical School		Patent, AdisInsight
1/23/2012	#202833	INGENOL MEBUTATE	LEO LABS	National Cancer Institute (US)/ University of Queensland (Australia)	Yes (no patent)	AdisInsight, Drug History
1/31/2012	#203188	IVACAFTOR	VERTEX PHARMS	Cystic Fibrosis Foundation Therapeutics		AdisInsight
3/6/2012	#021746	LUCINACTANT	WINDTREE THERAP	The Scripps Research Institute		Patent

4/6/2012	#202008	FLORBETAPIR F-18	AVID RADIOPHARMS INC	University of Pennsylvania (NIH)	Yes	Patent
8/27/2012	#203100	COBICISTAT; ELVITEGRAVIR; EMTRICITABINE***; TENOFVIR DISOPROXIL FUMARATE	GILEAD SCIENCES INC	Emory University (NIH)	Yes	Patent
8/31/2012	#203415	ENZALUTAMIDE	ASTELLAS	University of California (US Army, NIH)	Yes	Patent
9/12/2012	#203155	CHOLINE C-11	MCPRF	Mayo Clinic		Drug History
12/21/2012	#203441	TEDUGLUTIDE RECOMBINANT	NPS PHARMS INC	Toronto General Hospital; University of Toronto		Patent, AdisInsight
12/21/2012	#203858	LOMITAPIDE MESYLATE	AEGERION	University of Pennsylvania		Patent
1/25/2013	#022271	ALOGLIPTIN BENZOATE	TAKEDA PHARMS USA	Tufts College (NIH)	Yes	Patent
3/13/2013	#202207	TECHNETIUM TC-99M TILMANOCEPT	CARDINAL HEALTH 414	University of California (NIH)	Yes	Patent
10/25/2013	#203137	FLUTEMETAMOL F-18	GE HEALTHCARE	University of Pittsburgh		Patent
3/19/2014	#204684	MILTEFOSINE	KNIGHT THERAPS	Max-Planck (Germany)		Patent (Merck index)
3/19/2014	#204677	FLORBETABEN F-18	PIRAMAL IMAGING	University of Pennsylvania (NIH)	Yes	Patent



8/19/2014	#205494	ELIGLUSTAT TARTRATE	GENZYME CORP	University of Michigan (NIH)	Yes	Patent
12/19/2014	#206162	OLAPARIB	ASTRAZENECA PHARMS	University of Sheffield/Yorkshire Cancer Research/The Institute of Cancer Research/University of Cambridge (UK)		Patent, AdisInsight
12/19/2014	#206426	PERAMIVIR	BIOCRIST	University of Alabama		Patent, AdisInsight
4/29/2015	#206333	DEOXYCHOLIC ACID	KYTHERA BIOPHARMS	University of California		Patent
7/2/2015	#206038	IVACAFTOR; LUMACAFTOR	VERTEX PHARMS INC	Cystic Fibrosis Foundation Therapeutics		AdisInsight
10/23/2015	#207953	TRABECTEDIN	JANSSEN PRODS	University of Illinois		AdisInsight
11/5/2015	#207561	COBICISTAT; ELVITEGRAVIR; EMTRICITABINE****; TENOFVIR ALAFENAMIDE FUMARATE	GILEAD SCIENCES INC	Emory (NIH)	Yes	Patent
4/11/2016	#208573	VENETOCLAX	ABBVIE INC	The Walter and Eliza Hall Institute of Medical Research		Patent
5/27/2016	#208054	FLUCICLOVINE F-18	BLUE EARTH	Emory University (Department of Energy)	Yes	Patent
5/27/2016	#207999	OBETICHOLIC ACID	INTERCEPT PHARMS INC	University of Perugia (Italy)		AdisInsight

9/19/2016	#206488	ETEPLIRSEN	SAREPTA THERAPS INC	Leiden University Medical Center (Netherlands)/University of Western Australia		Patent
12/19/2016	#209115	RUCAPARIB CAMSYLATE	CLOVIS ONCOLOGY INC	Newcastle University (UK)/Cancer Research UK		Patent
12/23/2016	#209531	NUSINERSEN SODIUM	BIOGEN IDEC	University of Massachusetts (NIH)/ Cold Spring Harbor Laboratory	Yes	Patent
4/28/2017	#207997	MIDOSTAURIN	NOVARTIS PHARMS CORP	Dana Farber Cancer Institute		Patent
8/29/2017	#209570	BENZNIDAZOLE*****	CHEMO RESEARCH SL	Brazilian Government, Drugs for Neglected Diseases Initiative Foundation		Drug History
12/18/2017	#208254	NETARSUDIL DIMESYLATE	AERIE PHARMS INC	Duke University		Patent, AdisInsight
12/21/2017	#209360	ANGIOTENSIN II ACETATE	LA JOLLA PHARM CO	George Washington University		Patent

\* Considered to have US government contributions if the drug originated at US government lab, a patent was assigned to a US government agency, or a patent declared US government funding of the invention. Two drugs had origins with the National Cancer Institute, however we did not find patents held by the NCI.

\*\* Artemether and lumefantrine are both new molecular entities with public-sector origins. For our analysis this counts as one product.

\*\*\*This combination product contains the NME elvitegravir. However, it is included as having a public-sector origin as emtricitabine originated at Emory. This product represented the first time elvitegravir was approved by the FDA.

\*\*\*\* This combination product contains the NME tenofovir alafenamide fumarate (TAF). However, it is included as having a public-sector origin as emtricitabine originated at Emory. This product represented the first time TAF was approved by the FDA.

\*\*\*\*\*Benzimidazole represents a unique case. It was discovered through research at Hoffman-LaRoche and not through publicly-supported research. However, Hoffman-LaRoche donated the rights to the drug to the Brazilian government. In addition, the Drug for Neglected Diseases Initiative Foundation supported the development and FDA-approval of the drug in the US and is being sold on a “no profit no loss” basis.<sup>22</sup>

**Table 2: New drugs made by spin-off companies that were based on publicly-supported research contributions**

Approval Date	App No.	Drug Name (Generic)	Manufacturer	Spin-off Company	Public-sector institution	Source
1/18/2008	#022187	ETRAVIRINE*	JANSSEN R AND D	Tibotec	Rega Institute	AdisInsight
1/14/2011	#022454	IOFLUPANE I-123	GE HLTHCARE INC	Research Biochemicals International	Northeastern University	Patent
5/20/2011	#202022	RILPIVIRINE HYDROCHLORIDE*	JANSSEN PRODS	Tibotec	Rega Institute	AdisInsight
8/17/2011	#202429	VEMURAFENIB	HOFFMANN LA ROCHE	Plexxikon	Yale University / University of California-Berkeley.	Patent
7/20/2012	#202714	CARFILZOMIB	ONYX THERAP	Proteolix	Yale University / California Institute of Technology	Patent
8/30/2012	#202811	LINACLOTIDE	ALLERGAN SALES LLC	Microbia	Whitehead Institute	Patent
5/15/2013	#203971	RADIUM RA-223 DICHLORIDE	BAYER HLTHCARE	Anticancer Therapeutic Inventions	Norwegian Radium Hospital and the University of Oslo	Patent
12/6/2013	#204671	SOFOSBUVIR	GILEAD SCIENCES INC	Pharmasset	Emory University	Patent
7/7/2014	#204427	TAVABOROLE	ANACOR PHARMS INC	Anacor Pharmaceuticals	Stanford University/ Pennsylvania State University	Patent
10/10/2014	#205834	LEDIPASVIR**; SOFOSBUVIR	GILEAD SCIENCES INC	Pharmasset	Emory University	Patent
6/28/2016	#208341	SOFOSBUVIR; VELPATASVIR**	GILEAD SCIENCES INC	Pharmasset	Emory University	Patent
3/13/2017	#209092	RIBOCICLIB SUCCINATE	NOVARTIS PHARMS CORP	Astex Therapeutics	University of Cambridge	Patent

6/19/2017	#208610	DELAFLOXACIN MEGLUMINE	MELINTA	Melinta	Yale University	Patent
7/18/2017	#209195	SOFOSBUVIR; VELPATASVIR; VOXILAPREVIR**	GILEAD SCIENCES INC	Pharmasset	Emory University	Patent

\*Both etravirine and rilpivirine are nonnucleoside reverse transcriptase inhibitors and are successors to the TIBO compound discovered at the Rega Institute. This discovery led to the spin-off Tibotec (later bought by Johnson and Johnson and merged with its Janssen division).

\*\*Ledipasvir, velpatasvir, and voxilaprevir are all new molecular entities approved as combination products with a sofosbuvir backbone. Sofosbuvir is considered to have originated at the public-sector spin-off Pharmasset and therefore each of these products are considered to have a spin-off origin.

**Table 3: Characteristics of patents on drugs with origins in publicly-supported research contributions**

	<b>Direct public-sector contribution</b>	<b>Spin-off company based on public-sector contribution</b>	<b>Total</b>
<b>Number of drugs, N</b>	48	14	62
No public-sector or spin-off patents identified, N	10	2	12
<b>≥1 public-sector or spin-off patent(s) identified, N</b>	38	12	50
≥1 patent held by public-sector institution, N	30	0	30
≥1 patent held by public-sector spin-off, N	14	12	26
≥1 patent declares government funding, N	17	0	17
Share of patents held by public-sector or spin-off, % (95% CI) (N=38; N=12)	70 (60-81)	81 (64-98)	72 (63-81)
Public-sector or spin-off holds first patent, n (%) (N=38; N=12)	32 (84%)	12 (100%)	44 (88%)
<b>Number of drugs with Orange Book patent(s), N</b>	44	14	58
≥ 1 patent on drug substance, N	34	12	46
≥ 1 patent on drug product, N	38	12	50
≥ 1 patent on drug substance or product, N	41	13	54
<b>Drugs with ≥1 public-sector or spin-off patents listed in Orange Book, N</b>	35*	12	47
≥1 public-sector or spin-off patents on drug substance, N	25	10	35
≥1 public-sector or spin-off patent on drug product, N	21	9	30
≥1 public-sector or spin-off patent on drug product or substance, N	27	11	38

\*7 products had no patents on drug substance, 6 had no patents on drug product, 3 had no patents on either drug substance or drug product.

**Table 4: Regulatory designations and other FDA classifications**

	Publicly-supported, n (%)	Publicly-supported or spin-off, n (%)	Non-public-supported origin, n (%)	P-value**
<b>Total</b>	<b>48</b>	<b>62</b>	<b>186</b>	
Priority Review	26 (57%)	36 (58%)	78 (42%)	0.04
Breakthrough Therapy*	4 (8%)	8 (13%)	18 (10%)	0.48
Accelerated Approval	8 (17%)	10 (16%)	19 (10%)	0.25
Fast Track	14 (29%)	22 (35%)	52 (28%)	0.27
1 or more expedited FDA designation	31 (65%)	42 (68%)	87 (47%)	0.005
First in class	22 (46%)	28 (45%)	48 (26%)	0.007
Rare disease treatment	24 (50%)	26 (42%)	56 (30%)	0.09

\*The Breakthrough Therapy designation was established in 2012 by the FDA Safety and Innovation Act. The first new molecular entity received this designation in November 2013.

\*\*Fisher exact test of independence between publicly-supported + spin-off vs. non-public-sector.

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**Supplementary Table S1: FDA approved drugs containing a new molecular entity, 2008-2017**

Approval Date	Drug Name (Generic)	Manufacturer	App No.	Drug Class	FDA Approval Characteristics*	Data Source**
1/18/2008	ETRAVIRINE	JANSSEN R AND D	#022187	Infectious diseases	P, A	OB; M
2/29/2008	DESVENLAFAXINE SUCCINATE	WYETH PHARMS INC	#021992	Psychiatric	S	OB; M
3/20/2008	BENDAMUSTINE HYDROCHLORIDE	CEPHALON	#022249	Hematologic- Oncologic	P, O	OB; No M patent
4/10/2008	REGADENOSON	ASTELLAS	#022161	Diagnostic	S	OB; M
4/24/2008	METHYLNALTREXONE BROMIDE	SALIX PHARMS	#021964	Gastrointestinal	S, FIC	OB; M
5/20/2008	ALVIMOPAN	CUBIST PHARMS	#021775	Gastrointestinal	S	OB; M
6/23/2008	DIFLUPREDNATE	NOVARTIS PHARMS CORP	#022212	Ophthalmologic	P	OB; M
7/3/2008	GADOXETATE DISODIUM	BAYER HLTHCARE	#022090	Diagnostic	S	OB; M
8/1/2008	CLEVIDIPINE	CHIESI USA INC	#022156	Cardiologic	S	OB; M
8/15/2008	TETRABENAZINE	VALEANT PHARMS NORTH	#021894	Neurologic	P, O, FIC	No OB patent; M
9/19/2008	IOBENGUANE SULFATE I-123	GE HEALTHCARE	#022290	Diagnostic	P, O	No OB patent; M
10/8/2008	SILODOSIN	ALLERGAN SALES LLC	#022206	Genitourinary/ Renal	S	No OB patent; M
10/28/2008	LACOSAMIDE	UCB INC	#022253	Neurologic	S	OB; M

10/31/2008	FESOTERODINE FUMARATE	PFIZER	#022030	Genitourinary/ Renal	S	OB; M
11/14/2008	RUFINAMIDE	EISAI INC	#021911	Neurologic	S, O	OB; M
11/20/2008	TAPENTADOL HYDROCHLORIDE	DEPOMED INC	#022304	Neurologic	S	OB; M
11/20/2008	ELTROMBOPAG OLAMINE	NOVARTIS PHARMS CORP	#022291	Hematologic- Oncologic	P, O, A	OB; M
12/15/2008	PLERIXAFOR	GENZYME	#022311	Hematologic- Oncologic	P, O, FIC	OB; No M patent
12/22/2008	GADOFOSVESET TRISODIUM	LANTHEUS MEDCL	#021711	Diagnostic	S	OB; M
12/24/2008	DEGARELIX ACETATE	FERRING	#022201	Hematologic- Oncologic	S	OB; M
1/14/2009	MILNACIPRAN HYDROCHLORIDE	ALLERGAN SALES LLC	#022256	Psychiatric	S	OB; M
2/13/2009	FEBUXOSTAT	TAKEDA PHARMS USA	#021856	Metabolic / Endocrine	S	OB; M
3/30/2009	EVEROLIMUS	NOVARTIS	#022334	Hematologic- Oncologic	P	OB; M
4/7/2009	ARTEMETHER***; LUMEFANTRINE***	NOVARTIS	#022268	Infectious diseases	P, O, FT, FIC	OB; M
4/9/2009	BENZYL ALCOHOL	SHIONOGI INC	#022129	Infectious diseases	S	OB; No M patent
5/6/2009	ILOPERIDONE	VANDA PHARMS INC	#022192	Psychiatric	S	OB; M
5/19/2009	TOLVAPTAN	OTSUKA AMERICA PHARM	#022275	Genitourinary/ Renal	S	OB; M

5/28/2009	BESIFLOXACIN HYDROCHLORIDE	BAUSCH AND LOMB	#022308	Ophthalmologic	S	OB; M
7/1/2009	DRONEDARONE HYDROCHLORIDE	SANOVI AVENTIS US	#022425	Cardiologic	P	OB; M
7/10/2009	PRASUGREL HYDROCHLORIDE	ELI LILLY AND CO	#022307	Cardiologic	P	OB; M
7/31/2009	SAXAGLIPTIN HYDROCHLORIDE	ASTRAZENECA AB	#022350	Metabolic/ Endocrine	S	OB; M
8/13/2009	ASENAPINE MALEATE	FOREST LABS LLC	#022117	Psychiatric	S	OB; M
8/21/2009	VIGABATRIN	LUNDBECK PHARMS LLC	#020427	Neurologic	S, O	No OB patent; M
9/8/2009	BEPOTASTINE BESILATE		#022288	Ophthalmologic	S	OB; M
9/11/2009	TELAVANCIN HYDROCHLORIDE	THERAVANCE BIOPHARMA	#022110	Infectious diseases	S	OB; M
9/24/2009	PRALATREXATE	ALLOS	#022468	Hematologic- Oncologic	P, O, A	OB; M
10/19/2009	PAZOPANIB HYDROCHLORIDE	NOVARTIS PHARMS CORP	#022465	Hematologic- Oncologic	S	OB; M
11/5/2009	ROMIDEPSIN	CELGENE	#022393	Hematologic- Oncologic	S, O	OB; M
11/16/2009	CAPSAICIN	ACORDA	#022395	Neurologic	S, O	OB; No M patent
1/22/2010	DALFAMPRIDINE	ACORDA	#022250	Neurologic	P, O, FIC	OB; No M patent
1/25/2010	LIRAGLUTIDE RECOMBINANT	NOVO NORDISK INC	#022341	Metabolic / Endocrine	S	OB; M
2/26/2010	VELAGLUCERASE ALFA	SHIRE HUMAN GENETIC	#022575	Metabolic / Endocrine	P, O	No OB patent; M

3/18/2010	CARGLUMIC ACID	ORPHAN EUROPE	#022562	Metabolic / Endocrine	P, O, FT, FIC	No OB patent; No M patent
3/30/2010	POLIDOCANOL	CHEMISCH FBRK KRSSLR	#021201	Dermatology	S	No OB patent; No M patent
5/6/2010	DIENOGEST***; ESTRADIOL VALERATE	BAYER HLTHCARE	#022252	Women's Health	S	OB; M
6/17/2010	CABAZITAXEL	SANOVI AVENTIS US	#201023	Hematologic- Oncologic	P	OB; M
7/28/2010	ALCAFTADINE	ALLERGAN	#022134	Ophthalmologic	S	OB; No M entry
8/13/2010	ULIPRISTAL ACETATE	LAB HRA PHARMA	#022474	Women's Health	S	OB; M
9/21/2010	FINGOLIMOD	NOVARTIS	#022527	Neurologic	P, FIC	OB; M
10/19/2010	DABIGATRAN ETEXILATE MESYLATE	BOEHRINGER INGELHEIM	#022512	Hematologic- Oncologic	P	OB; M
10/28/2010	LURASIDONE HYDROCHLORIDE	SUNOVION PHARMS INC	#200603	Psychiatric	S	OB; M
10/29/2010	CEFTAROLINE FOSAMIL	ALLERGAN SALES LLC	#200327	Infectious diseases	S	OB; M
11/10/2010	TESAMORELIN ACETATE	THERATECHNOLOGIES	#022505	Metabolic / Endocrine	S, FIC	OB; M
11/15/2010	ERIBULIN MESYLATE	EISAI INC	#201532	Hematologic- Oncologic	P, FIC	OB; M
1/14/2011	IOFLUPANE I-123	GE HLTHCARE INC	#022454	Diagnostic	P	OB; M
1/18/2011	SPINOSAD	PARAPRO LLC	#022408	Infectious diseases	S	OB; No M patent
1/21/2011	VILAZODONE HYDROCHLORIDE	ALLERGAN SALES LLC	#022567	Psychiatric	S	OB; M
2/25/2011	AZILSARTAN KAMEDOXOMIL	ARBOR PHARMS LLC	#200796	Cardiologic	S	OB; M

2/28/2011	ROFLUMILAST	ASTRAZENECA PHARMS	#022522	Pulmonary	S, FIC	OB; M
3/14/2011	GADOBUTROL	BAYER HLTHCARE	#201277	Diagnostic	S	OB; M
4/6/2011	VANDETANIB	GENZYME CORP	#022405	Hematologic- Oncologic	P, O, FT	OB; M
4/6/2011	GABAPENTIN ENACARBIL	ARBOR PHARMS LLC	#022399	Psychiatric	S	OB; M
4/28/2011	ABIRATERONE ACETATE	JANSSEN BIOTECH	#202379	Hematologic- Oncologic	P, FIC	OB; M
5/2/2011	LINAGLIPTIN	BOEHRINGER INGELHEIM	#201280	Metabolic / Endocrine	S	OB; M
5/13/2011	BOCEPREVIR	MERCK SHARP DOHME	#202258	Infectious diseases	P, FT, FIC	OB; M
5/20/2011	RILPIVIRINE HYDROCHLORIDE	JANSSEN PRODS	#202022	Infectious diseases	S	OB; M
5/23/2011	TELAPREVIR	VERTEX PHARMS	#201917	Infectious diseases	P, FT	OB; M
5/27/2011	FIDAXOMICIN	CUBIST PHARMS LLC	#201699	Infectious diseases	P, FT	OB; M
6/10/2011	EZOGABINE	GLAXOSMITHKLINE	#022345	Neurologic	S, FIC	No OB patent; M
7/1/2011	INDACATEROL MALEATE	SUNOVION PHARMS INC	#022383	Pulmonary	S	OB; M
7/1/2011	RIVAROXABAN	JANSSEN PHARMS	#022406	Hematologic- Oncologic	S	OB; M
7/20/2011	TICAGRELOR	ASTRAZENECA PHARMS	#022433	Cardiologic	S	OB; M
8/17/2011	VEMURAFENIB	HOFFMANN LA ROCHE	#202429	Hematologic- Oncologic	P, O, FT, FIC	OB; M
8/25/2011	ICATIBANT ACETATE	SHIRE ORPHAN THERAP	#022150	Hematologic- Oncologic	P, O, FT, FIC	OB; M



8/26/2011	CRIZOTINIB	PF PRISM CV	#202570	Hematologic- Oncologic	P, O, A, FT, FIC	OB; M
10/14/2011	DEFERIPRONE	AOPHARMA INC	#021825	Hematologic- Oncologic	S, O, A, FT	OB; No M patent
10/21/2011	CLOBAZAM	LUNDBECK PHARMS LLC	#202067	Neurologic	S, O	No OB patent; M
11/16/2011	RUXOLITINIB PHOSPHATE	INCYTE CORP	#202192	Hematologic- Oncologic	P, O, FT, FIC	OB; M
1/23/2012	INGENOL MEBUTATE	LEO LABS	#202833	Dermatology	S, FIC	OB; M
1/27/2012	AXITINIB	PF PRISM CV	#202324	Hematologic- Oncologic	S, FT	OB; M
1/30/2012	VISMODEGIB	GENENTECH	#203388	Hematologic- Oncologic	P, FIC	OB; M
1/31/2012	IVACAFTOR	VERTEX PHARMS	#203188	Pulmonary	P, O, FT, FIC	OB; M
2/10/2012	TAFLUPROST	OAK PHARMS INC	#202514	Ophthalmologic	S	OB; M
3/6/2012	LUCINACTANT	WINDTREE THERAP	#021746	Pulmonary	S, FT	OB; No M entry
3/27/2012	PEGINESATIDE ACETATE	TAKEDA PHARMS USA	#202799	Hematologic- Oncologic	S	OB; M
4/6/2012	FLORBETAPIR F-18	AVID RADIOPHARMS INC	#202008	Diagnostic	P, FIC	OB; M
4/27/2012	AVANAFIL	METUCHEN PHARMS	#202276	Genitourinary/ Renal	S	OB; M
5/1/2012	TALIGLUCERASE ALFA	PFIZER	#022458	Metabolic / Endocrine	S, O, FT	OB; M
6/27/2012	LORCASERIN HYDROCHLORIDE	EISAI INC	#022529	Metabolic / Endocrine	S, FIC	OB; M
6/28/2012	MIRABEGRON	APGDI	#202611	Genitourinary/ Renal	S, FIC	OB; M

7/16/2012	CITRIC ACID; MAGNESIUM OXIDE; SODIUM PICOSULFATE***	FERRING PHARMS INC	#202535	Gastrointestinal	S	OB; No M entry
7/20/2012	CARFILZOMIB	ONYX THERAP	#202714	Hematologic- Oncologic	S, O, A, FT	OB; M
7/23/2012	ACLIDINIUM BROMIDE	ASTRAZENECA PHARMS	#202450	Pulmonary	S	OB; M
8/27/2012	COBICISTAT; ELVITEGRAVIR***; EMTRICITABINE; TENOFVIR DISOPROXIL FUMARATE	GILEAD SCIENCES INC	#203100	Infectious diseases	S, FT	OB; M
8/30/2012	LINACLOTIDE	ALLERGAN SALES LLC	#202811	Gastrointestinal	S, FIC	OB; M
8/31/2012	ENZALUTAMIDE	ASTELLAS	#203415	Hematologic- Oncologic	P, FT	OB; No M patent
9/4/2012	BOSUTINIB MONOHYDRATE	PF PRISM CV	#203341	Hematologic- Oncologic	S, O	OB; M
9/12/2012	TERIFLUNOMIDE	SANOVI AVENTIS US	#202992	Neurologic	S, FIC	OB; M
9/12/2012	CHOLINE C-11	MCPRF	#203155	Diagnostic	P, FIC	No OB patent; No M patent
9/27/2012	REGORAFENIB	BAYER HLTHCARE	#203085	Hematologic- Oncologic	P, FT	OB; M
10/22/2012	PERAMPANEL	EISAI INC	#202834	Neurologic	S, FIC	OB; M
10/26/2012	OMACETAXINE MEPESUCCINATE	TEVA PHARMS INTL	#203585	Hematologic- Oncologic	S, O, A, FIC	OB; M
11/6/2012	TOFACITINIB CITRATE	PF PRISM CV	#203214	Rheumatologic	S	OB; M

11/29/2012	CABOZANTINIB S-MALATE	EXELIXIS	#203756	Hematologic-Oncologic	P, O, FT, FIC	OB; M
12/14/2012	PONATINIB HYDROCHLORIDE	ARIAD	#203469	Hematologic-Oncologic	P, O, A, FT	OB; M
12/14/2012	PASIREOTIDE DIASPARTATE	NOVARTIS	#200677	Metabolic / Endocrine	S, O, FIC	OB; M
12/21/2012	TEDUGLUTIDE RECOMBINANT	NPS PHARMS INC	#203441	Gastrointestinal	S, O, FIC	OB; M
12/21/2012	LOMITAPIDE MESYLATE	AEGERION	#203858	Cardiologic	S, O, FIC	OB; No M patent
12/28/2012	APIXABAN	BRISTOL MYERS SQUIBB	#202155	Hematologic-Oncologic	P	OB; M
12/28/2012	BEDAQUILINE FUMARATE	JANSSEN THERAP	#204384	Infectious diseases	P, O, A, FT, FIC	OB; M
12/31/2012	CROFELEMER	NAPO PHARMS INC	#202292	Gastrointestinal	P, FT, FIC	OB; M
1/25/2013	ALOGLIPTIN BENZOATE	TAKEDA PHARMS USA	#022271	Metabolic / Endocrine	S	OB; M
1/29/2013	MIPOMERSEN SODIUM	KASTLE THERAPS LLC	#203568	Cardiologic	S, O, FIC	OB; M
2/8/2013	POMALIDOMIDE	CELGENE	#204026	Hematologic-Oncologic	S, O, A, FT	OB; M
2/26/2013	OSPEMIFENE	DUCHESNAY	#203505	Women's Health	S	OB; M
3/13/2013	TECHNETIUM TC-99M TILMANOCEPT	CARDINAL HEALTH 414	#202207	Diagnostic	S	OB; No M patent
3/20/2013	GADOTERATE MEGLUMINE	GUERBET	#204781	Diagnostic	P	No OB patent; M
3/27/2013	DIMETHYL FUMARATE	BIOGEN IDEC INC	#204063	Neurologic	S, FIC	OB; No M patent

3/29/2013	CANAGLIFLOZIN	JANSSEN PHARMS	#204042	Metabolic / Endocrine	S, FIC	OB; M
5/10/2013	FLUTICASONE FUROATE; VILANTEROL TRIFENATATE***	GLAXO GRP LTD	#204275	Pulmonary	S	OB; M
5/15/2013	RADIUM RA-223 DICHLORIDE	BAYER HLTHCARE	#203971	Hematologic- Oncologic	P, FT, FIC	OB; M
5/29/2013	TRAMETINIB DIMETHYL SULFOXIDE	NOVARTIS PHARMS CORP	#204114	Hematologic- Oncologic	S, O, FT, FIC	OB; M
5/29/2013	DABRAFENIB MESYLATE	NOVARTIS PHARMS CORP	#202806	Hematologic- Oncologic	S, O, FT	OB; M
7/12/2013	AFATINIB DIMALEATE	BOEHRINGER INGELHEIM	#201292	Hematologic- Oncologic	P, O, FT	OB; M
8/12/2013	DOLUTEGRAVIR SODIUM	VIIV HLTHCARE	#204790	Infectious diseases	P, FT	OB; M
9/30/2013	VORTIOXETINE HYDROBROMIDE	TAKEDA PHARMS USA	#204447	Psychiatric	S	OB; M
10/3/2013	BAZEDOXIFENE ACETATE***; ESTROGENS, CONJUGATED	WYETH PHARMS PFIZER	#022247	Women's Health	S	OB; M
10/8/2013	RIOCIGUAT	BAYER HLTHCARE	#204819	Pulmonary	P, O, FIC	OB; M
10/18/2013	MACITENTAN	ACTELION PHARMS LTD	#204410	Pulmonary	S, O	OB; M
10/25/2013	FLUTEMETAMOL F-18	GE HEALTHCARE	#203137	Diagnostic	S	OB; M
11/8/2013	ESLICARBAZEPINE ACETATE	SUNOVION PHARMS INC	#022416	Neurologic	S	OB; M

11/13/2013	IBRUTINIB	PHARMACYCLICS INC	#205552	Hematologic- Oncologic	P, O, A, B, FT, FIC	OB; M
11/14/2013	LULICONAZOLE	MEDICIS	#204153	Infectious diseases	S	OB; M
11/22/2013	SIMEPREVIR SODIUM	JANSSEN PRODS	#205123	Infectious diseases	P, FT	OB; M
12/6/2013	SOFOSBUVIR	GILEAD SCIENCES INC	#204671	Infectious diseases	P, B, FT, FIC	OB; M
12/18/2013	UMECLIDINIUM BROMIDE***; VILANTEROL TRIFENATATE	GLAXOSMITHKLINE	#203975	Pulmonary	S	OB; M
1/8/2014	DAPAGLIFLOZIN	ASTRAZENECA AB	#202293	Metabolic / Endocrine	S	OB; M
1/31/2014	TASIMELTEON	VANDA PHARMS INC	#205677	Psychiatric	P, O	OB; M
2/18/2014	DROXIDOPA	LUNDBECK NA LTD	#203202	Cardiologic	P, O, A, FT, FIC	No OB patent; M
3/19/2014	MILTEFOSINE	KNIGHT THERAPS	#204684	Infectious diseases	P, O, FT, FIC	No OB patent; M
3/19/2014	FLORBETABEN F-18	PIRAMAL IMAGING	#204677	Diagnostic	S	OB; M
3/21/2014	APREMILAST	CELGENE CORP	#205437	Rheumatologic	S, FIC	OB; M
4/29/2014	CERITINIB	NOVARTIS PHARMS CORP	#205755	Hematologic- Oncologic	P, O, A, B	OB; M
5/8/2014	VORAPAXAR SULFATE	ARALEZ PHARMS	#204886	Cardiologic	S, FT, FIC	OB; M
5/23/2014	DALBAVANCIN HYDROCHLORIDE	ALLERGAN SALES LLC	#021883	Infectious diseases	P, FT	OB; No M patent
6/6/2014	EFINACONAZOLE	DOW PHARM	#203567	Dermatology	S	OB; M
6/20/2014	TEDIZOLID PHOSPHATE	CUBIST PHARMS LLC	#205435	Infectious diseases	P	OB; M
7/3/2014	BELINOSTAT	SPECTRUM PHARMS	#206256	Hematologic- Oncologic	P, O, A, FT	OB; M
7/7/2014	TAVABOROLE	ANACOR PHARMS INC	#204427	Dermatology	S, FIC	OB; M

7/23/2014	IDELALISIB	GILEAD SCIENCES INC	#205858	Hematologic- Oncologic	S, O, A, B, FT, FIC	OB; M
7/31/2014	OLODATEROL HYDROCHLORIDE	BOEHRINGER INGELHEIM	#203108	Pulmonary	S	OB; M
8/1/2014	EMPAGLIFLOZIN	BOEHRINGER INGELHEIM	#204629	Metabolic / Endocrine	S	OB; M
8/6/2014	ORITAVANCIN DIPHOSPHATE	MELINTA THERAP	#206334	Infectious diseases	P	OB; M
8/13/2014	SUVOREXANT	MERCK SHARP DOHME	#204569	Psychiatric	S, FIC	OB; M
8/19/2014	ELIGLUSTAT TARTRATE	GENZYME CORP	#205494	Metabolic / Endocrine	P, O	OB; M
9/16/2014	NALOXEGOL OXALATE	ASTRAZENECA PHARMS	#204760	Gastrointestinal	S	OB; No M entry
10/10/2014	NETUPITANT***; PALONOSETRON HYDROCHLORIDE	HELSINN HLTHCARE	#205718	Gastrointestinal	S	OB; M
10/10/2014	LEDIPASVIR***; SOFOSBUVIR	GILEAD SCIENCES INC	#205834	Infectious diseases	P, B, FT, FIC	OB; No M entry
10/10/2014	SULFUR HEXAFLUORIDE LIPID-TYPE A MICROSPHERES	BRACCO	#203684	Diagnostic	S	OB; No M patent
10/15/2014	PIRFENIDONE	GENENTECH INC	#022535	Pulmonary	P, O, B, FT, FIC	OB; M
10/15/2014	NINTEDANIB ESYLATE	BOEHRINGER INGELHEIM	#205832	Pulmonary	P, O, B, FT, FIC	OB; M
12/17/2014	FINAFLOXACIN	NOVARTIS PHARMS CORP	#206307	Infectious diseases	P	OB; M

12/19/2014	OLAPARIB	ASTRAZENECA PHARMS	#206162	Hematologic- Oncologic	P, O, A, FIC	OB; M
12/19/2014	PERAMIVIR	BIOCRYS	#206426	Infectious diseases	S, FT	OB; M
12/19/2014	DASABUVIR SODIUM***; OMBITASVIR***; PARITAPREVIR***; RITONAVIR	ABBVIE INC	#206619	Infectious diseases	P, B, FT, FIC	OB; M
12/19/2014	CEFTOLOZANE SULFATE***; TAZOBACTAM SODIUM	CUBIST PHARMS LLC	#206829	Infectious diseases	P, FT	OB; M
1/8/2015	EDOXABAN TOSYLATE	DAIICHI SANKYO INC	#206316	Hematologic- Oncologic	S	OB; M
2/3/2015	PALBOCICLIB	PFIZER INC	#207103	Hematologic- Oncologic	P, A, B, FIC	OB; M
2/13/2015	LENVATINIB MESYLATE	EISAI INC	#206947	Hematologic- Oncologic	P, O	OB; M
2/23/2015	PANOBINOSTAT LACTATE	NOVARTIS PHARMS CORP	#205353	Hematologic- Oncologic	P, O, A	OB; M
2/25/2015	AVIBACTAM SODIUM***; CEFTAZIDIME	ALLERGAN SALES LLC	#206494	Infectious diseases	P, FT	OB; No M entry
3/6/2015	ISAVUCONAZONIUM SULFATE	ASTELLAS	#207500	Infectious diseases	P, O	OB; M
3/17/2015	CHOLIC ACID	RTRX	#205750	Gastrointestinal	P, O	No OB patent; No M entry
4/15/2015	IVABRADINE HYDROCHLORIDE	AMGEN INC	#206143	Cardiologic	P, FT, FIC	OB; M

4/29/2015	DEOXYCHOLIC ACID	KYTERA BIOPHARMS	#206333	Dermatology	S	OB; M
5/27/2015	ELUXADOLINE	ALLERGAN HOLDINGS	#206940	Gastrointestinal	P, FT	OB; M
6/22/2015	CANGRELOR	CHIESI USA INC	#204958	Cardiologic	S	OB; M
7/2/2015	IVACAFTOR; LUMACAFTOR***	VERTEX PHARMS INC	#206038	Pulmonary	P, O, B, FT, FIC	OB; No M entry
7/7/2015	SACUBITRIL***; VALSARTAN	NOVARTIS PHARMS CORP	#207620	Cardiologic	P, FT, FIC	OB; No M entry
7/10/2015	BREXPIRAZOLE	OTSUKA PHARM CO LTD	#205422	Psychiatric	S	OB; M
7/24/2015	DACLATASVIR DIHYDROCHLORIDE	BRISTOL-MYERS SQUIBB	#206843	Infectious diseases	P, FT	OB; M
7/24/2015	SONIDEGIB PHOSPHATE	SUN PHARMA GLOBAL	#205266	Hematologic- Oncologic	S	OB; M
8/18/2015	FLIBANSERIN	SPROUT PHARMS	#022526	Women's Health	S, FIC	OB; M
9/1/2015	ROLAPITANT HYDROCHLORIDE	TESARO INC	#206500	Gastrointestinal	S	OB; No M patent
9/4/2015	URIDINE TRIACETATE	WELLSTAT THERAP	#208169	Metabolic / Endocrine	P, O, B, FIC	OB; M
9/17/2015	CARIPRAZINE HYDROCHLORIDE	ALLERGAN SALES LLC	#204370	Psychiatric	S	OB; M
9/22/2015	TIPIRACIL HYDROCHLORIDE***; TRIFLURIDINE	TAIHO ONCOLOGY	#207981	Hematologic- Oncologic	S, FT	OB; No M entry
9/25/2015	INSULIN DEGLUDEC	NOVO NORDISK INC	#203314	Metabolic / Endocrine	S	OB; M
10/5/2015	ARIPIRAZOLE LAUROXIL	ALKERMES INC	#207533	Psychiatric	S	OB; M



10/21/2015	PATIROMER SORBITE CALCIUM	RELYPSA INC	#205739	Gastrointestinal	S	OB; M
10/23/2015	TRABECTEDIN	JANSSEN PRODS	#207953	Hematologic- Oncologic	P, O	OB; No M entry
11/5/2015	COBICISTAT; ELVITEGRAVIR; EMTRICITABINE; TENOFVIR ALAFENAMIDE FUMARATE***	GILEAD SCIENCES INC	#207561	Infectious diseases	S, FT	OB; M
11/10/2015	COBIMETINIB FUMARATE	GENENTECH INC	#206192	Hematologic- Oncologic	P, O, FT	OB; M
11/13/2015	OSIMERTINIB MESYLATE	ASTRAZENECA PHARMS	#208065	Hematologic- Oncologic	P, O, A, B, FT	OB; M
11/20/2015	IXAZOMIB CITRATE	MILLENNIUM PHARMS	#208462	Hematologic- Oncologic	P, O	OB; M
12/11/2015	ALECTINIB HYDROCHLORIDE	HOFFMANN-LA ROCHE	#208434	Hematologic- Oncologic	P, O, A, B	OB; M
12/15/2015	SUGAMMADEX SODIUM	ORGANON SUB MERCK	#022225	Anesthesia	P, FIC	OB; M
12/21/2015	SELEXIPAG	ACTELION PHARMS LTD	#207947	Pulmonary	S, O	OB; M
12/22/2015	LESINURAD	IRONWOOD PHARMS INC	#207988	Metabolic / Endocrine	S	OB; M
1/28/2016	ELBASVIR***; GRAZOPREVIR***	MERCK SHARP DOHME	#208261	Infectious diseases	P, B	OB; M
2/18/2016	BRIVARACETAM	UCB INC	#205836	Neurologic	S	OB; M

3/30/2016	DEFIBROTIDE SODIUM	JAZZ PHARMS INC	#208114	Hematologic- Oncologic	P, O, FT, FIC	No OB patent; M
4/11/2016	VENETOCLAX	ABBVIE INC	#208573	Hematologic- Oncologic	P, O, A, B, FIC	OB; M
4/29/2016	PIMAVANSERIN TARTRATE	ACADIA PHARMS INC	#207318	Psychiatric	P, B	OB; M
5/27/2016	FLUCICLOVINE F-18	BLUE EARTH	#208054	Diagnostic	P	OB; No M entry
5/27/2016	OBETICHOLIC ACID	INTERCEPT PHARMS INC	#207999	Gastrointestinal	P, O, A, FT, FIC	OB; M
6/1/2016	GALLIUM DOTATATE GA-68	AAA USA INC	#208547	Diagnostic	P, O	No OB patent; M
6/28/2016	SOFOSBUVIR; VELPATASVIR***	GILEAD SCIENCES INC	#208341	Infectious diseases	P, B, FT	OB; M
7/11/2016	LIFITEGRAST	SHIRE DEV LLC	#208073	Ophthalmologic	P, FIC	OB; M
7/27/2016	LIXISENATIDE	SANOFI-AVENTIS US	#208471	Metabolic / Endocrine	S	OB; M
9/19/2016	ETEPLIRSEN	SAREPTA THERAPS INC	#206488	Neurologic	P, O, A, FT, FIC	OB; No M entry
12/14/2016	CRISABOROLE	ANACOR PHARMS INC	#207695	Dermatology	S	OB; M
12/19/2016	RUCAPARIB CAMSYLATE	CLOVIS ONCOLOGY INC	#209115	Hematologic- Oncologic	P, O, A, B	OB; M
12/23/2016	NUSINERSEN SODIUM	BIOGEN IDEC	#209531	Neurologic	P, O, FT, FIC	OB; M
1/19/2017	PLECANATIDE	SYNERGY PHARMS	#208745	Gastrointestinal	S	OB; M
2/7/2017	ETELCALCETIDE	KAI PHARMS INC	#208325	Metabolic / Endocrine	S	OB; M
2/9/2017	DEFLAZACORT	PTC THERAP	#208684	Neurologic	P, O, FT, FIC	No OB patent; M
2/28/2017	TELOTRISTAT ETIPRATE	LEXICON PHARMS INC	#208794	Gastrointestinal	P, O, FT, FIC	OB; M

3/13/2017	RIBOCICLIB SUCCINATE	NOVARTIS PHARMS CORP	#209092	Hematologic- Oncologic	P, B	OB; M
3/21/2017	SAFINAMIDE MESYLATE	US WORLDMEDS LLC	#207145	Neurologic	S	OB; M
3/23/2017	NALDEMEDINE TOSYLATE	SHIONOGI INC	#208854	Gastrointestinal	S	OB; M
3/27/2017	NIRAPARIB TOSYLATE	TESARO INC	#208447	Hematologic- Oncologic	P, O, B, FT	OB; M
4/3/2017	DEUTETRABENAZINE	TEVA BRANDED PHARM	#208082	Neurologic	S, O	OB; No M entry
4/11/2017	VALBENAZINE TOSYLATE	NEUROCRINE	#209241	Psychiatric	P, B, FT	OB; M
4/28/2017	BRIGATINIB	ARIAD	#208772	Hematologic- Oncologic	P, O, A, B	OB; No M entry
4/28/2017	MIDOSTAURIN	NOVARTIS PHARMS CORP	#207997	Hematologic- Oncologic	P, O, B, FT, FIC	OB; M
4/28/2017	ABALOPARATIDE	RADIUS HEALTH INC	#208743	Women's Health	S	OB; M
5/5/2017	EDARAVONE	MITSUBISHI TANABE	#209176	Neurologic	S, O, FIC	OB; No M patent
6/19/2017	DELAFLOXACIN MEGLUMINE	MELINTA	#208610	Infectious diseases	P, FT	OB; M
6/23/2017	BETRIXABAN	PORTOLA PHARMS INC	#208383	Hematologic- Oncologic	P, FT	OB; M
7/17/2017	NERATINIB MALEATE	PUMA BIOTECH	#208051	Hematologic- Oncologic	S	OB; M
7/18/2017	SOFOSBUVIR; VELPATASVIR; VOXILAPREVIR***	GILEAD SCIENCES INC	#209195	Infectious diseases	P, FT	OB; M

8/1/2017	ENASIDENIB MESYLATE	CELGENE CORP	#209606	Hematologic- Oncologic	P, O, FT, FIC	OB; No M entry
8/3/2017	GLECAPREVIR***; PIBRENTASVIR***	ABBVIE INC	#209394	Infectious diseases	P, B, FT	OB; M
8/29/2017	BENZNIDAZOLE	CHEMO RESEARCH SL	#209570	Infectious diseases	P, O, A	No OB patent; M
8/29/2017	MEROPENEM; VABORBACTAM***	REMPEX PHARMS	#209776	Infectious diseases	P, FT	OB; M
9/14/2017	COPANLISIB DIHYDROCHLORIDE	BAYER HEALTHCARE	#209936	Hematologic- Oncologic	P, O, A, FT	OB; M
9/15/2017	SECNIDAZOLE	LUPIN	#209363	Infectious diseases	P, FT	No OB patent; M
9/28/2017	ABEMACICLIB	ELI LILLY AND CO	#208716	Hematologic- Oncologic	P, B, FT	OB; M
10/31/2017	ACALABRUTINIB	ASTRAZENECA	#210259	Hematologic- Oncologic	P, O, A, B	OB; M
11/2/2017	LATANOPROSTENE BUNOD	BAUSCH AND LOMB	#207795	Ophthalmologic	S	OB; No M entry
11/8/2017	LETERMOVIR	MERCK SHARP DOHME	#209939	Infectious diseases	P, O, B, FT, FIC	OB; No M entry
12/5/2017	SEMAGLUTIDE	NOVO NORDISK INC	#209637	Metabolic / Endocrine	S	OB; No M entry
12/11/2017	OZENOXACIN	FERRER INTERNACIONAL	#208945	Infectious diseases	S	OB; M
12/18/2017	NETARSUDIL DIMESYLATE	AERIE PHARMS INC	#208254	Ophthalmologic	S, FIC	OB; No M entry
12/19/2017	ERTUGLIFLOZIN	MERCK SHARP DOHME	#209803	Metabolic / Endocrine	S	No OB patent; No M entry

12/20/2017	MACIMORELIN ACETATE	STRONGBRIDGE IRELAND	#205598	Diagnostic	S, O, FIC	OB; No M entry
12/21/2017	ANGIOTENSIN II ACETATE	LA JOLLA PHARM CO	#209360	Cardiologic	P, FIC	OB; No M patent

\*Represents designations by the Food and Drug Administration (FDA) as follows: S – standard approval, P – priority approval, O – orphan drug designation, A – accelerated approval, B – breakthrough designation, FT – fast track designation, FIC – first in class.

\*\*OB – At least one patent listed in the FDA Orange Book. M – At least one patent listed in the drug’s Merck Index entry.  
AdisInsight entries were available for all drugs except citric acid/magnesium oxide/sodium picosulfate (prepopik) and choline C-11.

\*\*\*Identifies the new molecular entity for combination products.

**Supplementary Table S2: New approvals and origins by drug class**

Drug Class	Publicly-supported	Publicly-supported spin-off	Public-sector and spin-off total	Total Approvals
Diagnostic	9	1	10	16
Anesthetic	0	0	0	1
Cardiologic	2	0	2	13
Dermatologic	2	1	3	6
Gastrointestinal	3	1	4	16
Genitourinary/Renal	0	0	0	5
Hematologic-Oncologic	13	4	17	64
Infectious diseases	6	7	13	39
Metabolic/Endocrine	3	0	3	22
Neurologic	5	0	5	21
Ophthalmologic	1	0	1	8
Psychiatric	0	0	0	15
Pulmonary	3	0	3	14
Rheumatologic	0	0	0	2
Women's health	1	0	1	6
<b>Total</b>	<b>48</b>	<b>14</b>	<b>62</b>	<b>248</b>

## Appendix: List of Drugs and Data

EXAMPLE:

Generic Name

- a. Orange Book Patent
- b. Merck Index
- c. Adis Insight
- d. Additional search Data

Name highlighted as follows: **QUESTIONABLE**, **PSRI ORIGIN CLASSIFICATION**, **PSRI SPIN OFF CLASSIFICATION**

### 1. ETRAVIRINE

- a. Janssen Pharmaceutica NV
- b. WO 0027825; eidem, US 7037917 (2000, 2006, both to Janssen)
- c. Originator Tibotec Pharmaceuticals
- d. Tibotec founded to work on TIBO compounds, discovered at **Rega Institute for Medical Research**.
- e. <https://pubs-acscs-org.ezp-prod1.hul.harvard.edu/doi/pdf/10.1021/jm040127p>

### 2. DESVENLAFAXINE SUCCINATE

- a. Wyeth
- b. US 4535186 (1984, 1985 both to Am. Home Prod.);
- c. Originator Wyeth
- d. Derivative of venlafaxine

### 3. BENDAMUSTINE HYDROCHLORIDE

- a. Cephalon, Inc.
- b. No patent
- c. Originator Jenapharm
- d. Bendamustine was first synthesized in 1963 by Ozegowski and Krebs (Institute for Microbiology and Experimental Therapy) in East Germany (the former German Democratic Republic). Until 1990 it was available only in East Germany. East German investigators found that it was useful for treating chronic lymphocytic leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and lung cancer. <https://en.wikipedia.org/wiki/Bendamustine> ; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3117628/>

### 4. REGADENOSON

- a. CV Therapeutics, Inc.; Gilead Palo Alto, Inc.; Gilead Sciences, Inc.
- b. US 6403567 (2000, 2002 both to CV Therapeutics).
- c. Originator CV Therapeutics
- d. CV Therapeutics; CVT 3146
- e. CV Therapeutics a spin off of two Washington university faculty (Louise Lange - Washington University; Peter G. Milner - Washington University) in 1992.
- f. **Likely independently found**

### 5. METHYLNALTREXONE BROMIDE

- a. Progenics Pharmaceuticals Inc.; UR Labs, Inc.; The University of Chicago; Wyeth; Wyeth LLC

- b. US 4176186 (1979 to Boehringer Ing.)
  - c. Originator University of Chicago
  - d. University of Chicago, PHS/HHS
6. ALVIMOPAN
- a. Adolor Corporation; Eli Lilly and Company
  - b. US 5250542 (1992, 1993 both to Lilly);
  - c. Originator Eli Lilly
  - d. <https://www.nature.com/articles/nrd2668#ref4> : “One such research programme resulted in the discovery of alvimopan<sup>4,5</sup>”
  - e. Eli Lilly: <https://pubs.acs.org/doi/abs/10.1021/jm00041a003> (1994)
  - f. Later UWash researchers (also PPD, Inc), funded by Aldor, Inc, published small clinical trial (2001)
7. DIFLUPREDNATE
- a. Senju Pharm
  - b. US 3780177 (1968, 1973 both to Warner-Lambert);
  - c. Originator Senju Pharmaceutical
  - d. synthetic difluorinated prednisolone derivative
  - e. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2709030/> : Originally designed for dermatologic indications  
<https://www.ncbi.nlm.nih.gov/pubmed/16485880/>; then adapted for ophthalmological indication  
<https://www.ncbi.nlm.nih.gov/pubmed/16023810/> (Senju)
8. GADOXETATE DISODIUM
- a. Bayer; Schering Aktiengesellschaft
  - b. US 5695739 (1991, 1997 both to Schering AG).
  - c. Originator Massachusetts General Hospital
  - d. Patents: 4899755
  - e. Verification: Patent
9. CLEVIDIPINE
- a. ASEA Aktiebolag; The Medicines Company
  - b. WO 9512578; eidem, US 5856346 (1995, 1999 both to Astra).
  - c. Originator AstraZeneca
  - d.
10. TETRABENAZINE
- a. No patent
  - b. US 2830993 (1958 to Hoffmann-La Roche);
  - c. Originator LifeHealth Limited
  - d. The compound has been known since the 1950s. by O Schneider and A Brossi at the research laboratory of Hoffmann-La Roche in Basel.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2656291/>
11. IOBENGUANE SULFATE I-123
- a. No patent
  - b. US 4584187 (1986 - Donald M. Wieland, Lawrence E. Brown, William H. Beierwaltes, Jiann-Long Wu (University of Michigan); Contract No. DE-AC02-76EV02031 awarded by the U.S. Department of Energy.
  - c. Originator GE Healthcare



## 12. SILODOSIN

- a. Kissei Pharmaceutical Co., Ltd.; Nippondenso Co., Ltd.; Synaptic Pharmaceutical Corporation
- b. US 5387603 (1994, 1995 both to Kissei)
- c. Originator Kissei Pharmaceutical
- d. At the start of the 1990s, Kissei Pharmaceutical Co., Ltd . began development of a1- AR antagonists highly selective to the LUT without affecting blood pressure [24,25].
- e. <https://onlinelibrary-wiley-com.ezp-prod1.hul.harvard.edu/doi/pdf/10.1002/9781118219683.ch14>

## 13. LACOSAMIDE

- a. Patent: RESEARCH CORPORATION TECHNOLOGIES (NIH Funding) ; to Harold Kohn (University of Houston)
- b. US 5773475 (1997, 1998 both to Research Corp. Technol.).
- c. Adis: University of Houston
- d. Lacosamide was discovered by Dr. Harold Kohn, Dr. Shridhar Andurkar, and colleagues at the University of Houston in 1996.  
<https://www.ncbi.nlm.nih.gov/pubmed/8627614>
- e. <https://pharmacy.unc.edu/news/2017/01/06/kohn-named-fellow-national-academy-inventors/>

## 14. FESOTERODINE FUMARATE

- a. Schwarz Pharma S.L.; U3 Pharma GmbH
- b. US 6713464 (1999, 2004 both to Schwarz).
- c. Originator Schwarz Pharma
- d. Fesoterodine is a prodrug. It is broken down into its active metabolite, desfesoterodine, by plasma esterases.

## 15. RUFINAMIDE

- a. Novartis AG
- b. US 4789680 (1986, 1988 both to Ciba-Geigy).
- c. Originator Novartis

## 16. TAPENTADOL HYDROCHLORIDE

- a. Gruenthal GmbH; NPS Pharmaceuticals, Inc.
- b. US 6248737; US RE39593 (1996, 2001, 2007 all to Grünenthal).
- c. Originator Gruenthal
- d.

## 17. ELTROMBOPAG OLAMINE

- a. GlaxoSmithKline; SmithKline Beecham Corporation; SmithKline Beecham Corporation; Glaxo Group Limited
- b. US 7160870 (2001, 2008 both to SmithKline Beecham; Glaxo).
- c. Originator **Ligand Pharmaceuticals**
- d. Ligand Pharmaceuticals was founded, as Progenx Inc., in 1987 by by Brook Byers and went
- e. Probably too long to really be spin off

## 18. PLERIXAFOR

- a. Anormed Inc.; Genzyme Corporation; Johnson Matthey Public Limited Company
- b. No patent

- c. Originator: Genzyme Corporation; Rega Institute for Medical Research;
- d. Verified: AMD3100 ; Erik De Clercq (Rega Institute)  
[https://docs.wixstatic.com/ugd/b8cb99\\_a3bd842290b74232a403bff394b31855.pdf](https://docs.wixstatic.com/ugd/b8cb99_a3bd842290b74232a403bff394b31855.pdf)
- e. Preparation:  
<https://pubs.acs.org/doi/abs/10.1021/ic00268a022?journalCode=inocaj>
- f. Originally discovered in 1987 to carry out basic studies on redox chemistry. Then thought to be used as treatment for HIV, now used to mobilize hematopoietic stem cells

#### 19. GADOFOSVESET TRISODIUM

- a. Epix Pharmaceuticals.; Lantheus Medical Imaging, Inc.; Schering Aktiengesellschaft
- b. WO 9623526 (1996 to Epix Medical).
- c. Originator Massachusetts General Hospital
- d. Epix is a spin off of Harvard Medical School/MGH.  
[https://www.massgeneral.org/imaging/news/radrounds/june\\_2012/](https://www.massgeneral.org/imaging/news/radrounds/june_2012/)

#### 20. DEGARELIX ACETATE

- a. Ferring BV
- b. US 5925730 (1998, 1999 both to Ferring);
- c. Originator Ferring Pharmaceuticals

#### 21. MILNACIPRAN HYDROCHLORIDE

- a. Cypress Bioscience, Inc.
- b. US 4478836 (1983, 1984 both to Pierre Fabre);
- c. Originator Pierre Fabre
- d. Cypress bought rights to drug in 2003 from Pierre Fabre

#### 22. FEBUXOSTAT

- a. Takeda Pharmaceuticals U.S.A., Inc.; Teijin Limited
- b. US 5614520 (1992, 1997 both to Teijin).
- c. Originator Teijin Pharma

#### 23. EVEROLIMUS

- a. Novartis AG; Novartis Pharmaceuticals Corporation; Sandoz Ltd.
- b. US 5665772 (1994, 1997 both to Sandoz).
- c. Originator Novartis; University of Michigan Comprehensive Cancer Center
- d. No listing of source of why Michigan is originator or owner.
- e. Likely a mistake

#### 24. ARTEMETHER; LUMEFANTRINE

- a. Ciba-Geigy AG; Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences
- b. CN 1042535 (1990 to Acad. Military Med. Sci., Microbiol. & Epidemic Dis. Instit.).
- c. Originator Academy of Military Medical Sciences (Beijing)

#### 25. BENZYL ALCOHOL

- a. Summers Laboratories, Inc.
- b. No merck patent
- c. Originator Summers Laboratories

#### 26. ILOPERIDONE

- a. Aventis Pharmaceuticals Inc.; Vanda Pharmaceuticals, Inc.

- b. US 5364866 (1990, 1994 both to Hoechst-Roussel);
  - c. Originator sanofi-aventis
27. TOLVAPTAN
- a. OTSUKA PHARMACEUTICAL CO., LTD.
  - b. US 5258510 (1991, 1993 both to Otsuka);
  - c. Originator Otsuka America Pharmaceutical; Otsuka Pharmaceutical
28. BESIFLOXACIN HYDROCHLORIDE
- a. Bausch & Lomb Incorporated; SS Pharmaceutical Co., Ltd.; SSP Co. Ltd.; InSite Vision Incorporated
  - b. US 5447926 (1992, 1995 both to SS Pharma).
  - c. Originator InSite Vision; SSP Co
29. DRONEDARONE HYDROCHLORIDE
- a. Sanofi; sanofi-aventis
  - b. US 5223510 (1992, 1993 both to Sanofi).
  - c. Originator sanofi-aventis
30. PRASUGREL HYDROCHLORIDE
- a. Daiichi Sankyo Company, Limited; Sankyo Company, Limited; UbÄ“ Industries, Ltd.; Sankyo Company, Limited; Ube Industries, Ltd.; UbÄ“ Industries, Ltd.; Daiichi Sankyo Company, Limited
  - b. US 5288726 (1993, 1994 to Sankyo).
  - c. Originator Daiichi Sankyo Company; Ube Industries
31. SAXAGLIPTIN HYDROCHLORIDE
- a. Bristol-Myers Squibb Company
  - b. US 6395767 (2001, 2002 both to Bristol-Myers Squibb).
  - c. Originator Bristol-Myers Squibb
32. ASENAPINE MALEATE
- a. Akzo Nobel N.V.; N.V. Organon
  - b. US 4145434 (1979 to Akzona).
  - c. Originator Organon
33. VIGABATRIN
- a. No patent
  - b. US 3960927 (1975 -Richardson-Merrell [ Aventis ] )
  - c. Originator sanofi-aventis
34. BEPOTASTINE BESILATE
- a. Senju Pharmaceutical Co., Ltd.; UbÄ“ Industries, Ltd.; Tanabe Seiyaku Co., Ltd.
  - b. US 4929618 (1989, 1990 both to Ube).
  - c. Originator Ube Industries
35. TELAVANCIN HYDROCHLORIDE
- a. Theravance, Inc.
  - b. US 6635618 (2001, 2003 both to Advanced Medicine).
  - c. Originator Theravance
  - d. Founded in 1996. Originally as Advanced Medicine, Inc. George M. Whitesides (Harvard), John Griffin Ph.D. (Stanford professor at time of founding). Mathai Mammen (Janssen). Spun out Theravance Biopharma in 2013.
36. PRALATREXATE

- a. Sloan-Kettering Institute for Cancer Research; Southern Research Institute; SRI International; Sloan-Kettering Institute for Cancer Research
  - b. US 5354751 (1994 to SRI); US 6028071 (2000 to Sloan-Kettering
  - c. Inst. Cancer Res.).
  - d. Originator Memorial Sloan-Kettering Cancer Center; Southern Research Institute; SRI International
37. PAZOPANIB HYDROCHLORIDE
- a. GlaxoSmithKline; SmithKline Beecham Corporation
  - b. US 7105530 (2006 to SKB);
  - c. Originator GlaxoSmithKline
38. ROMIDEPSIN
- a. Astellas Pharma Inc.; Fujisawa Pharmaceutical Co., Ltd.
  - b. US 4977138 (both 1990 to Fujisawa).
  - c. Originator Astellas Pharma
  - d. The first total synthesis of romidepsin was accomplished by Harvard researchers and published in 1996.[4] Its mechanism of action was elucidated in 1998, when researchers from Fujisawa and the University of Tokyo found it to be a histone deacetylase inhibitor with effects similar to those of trichostatin A.[5] <https://en.wikipedia.org/wiki/Romidepsin>
39. CAPSAICIN
- a. The Regents of the University of California
  - b. No patent
  - c. Originator NeurogesX
40. DALFAMPRIDINE
- a. Acorda Therapeutics, Inc.; Elan Corporation, P.L.C.
  - b. No patent
  - c. Originator Elan Drug Technologies
  - d. Perdue Technology transfer claims the drugs origin
41. LIRAGLUTIDE RECOMBINANT
- a. Novo Nordisk A/S
  - b. WO 9808871; idem et al., US 6268343 (1998, 2001 both to Novo Nordisk)
  - c. Originator Novo Nordisk
42. VELAGLUCERASE ALFA
- a. NA
  - b. WO 0215927 (2002, Transkaryotic Therapy); US 7138262 (2006, Shire Human Genetic Ther.)
  - c. Originator Shire Pharmaceuticals Group
43. CARGLUMIC ACID
- a. NA
  - b. No patent
  - c. Originator Orphan Europe
44. POLIDOCANOL
- a. NA
  - b. No patent
  - c. Originator Chemische Fabrik Kreussler & Co
45. DIENOGEST; ESTRADIOL VALERATE

- a. Bayer Pharma Aktiengesellschaft; Jenapharm GmbH & Co. KG
  - b. US 4167517 (1977, 1979 both to VEB Jenapharm
  - c. Originator Bayer Schering Pharma
46. CABAZITAXEL
- a. Aventis Pharma S.A.; Rhone-Poulenc Rorer S.A.
  - b. 5847170 (1996, 1998 both to Rhone Poulenc Rorer).
  - c. Originator sanofi-aventis
47. ALCAFTADINE
- a. Janssen Pharmaceutica NV; Vistakon Pharmaceuticals, LLC
  - b. No entry
  - c. Originator Vistakon Pharmaceuticals
48. ULIPRISTAL ACETATE
- a. Laboratoire HRA-Pharma; The United States of America, as Represented by the Secretary, Department of Health and Human Services; Laboratoire HRA-Pharma
  - b. WO 8912448; eidem, US 4954490 (1989, 1990 both to Research Triangle Inst.).
  - c. Originator HRA Pharma; National Institutes of Health (USA)
49. FINGOLIMOD
- a. Novartis AG; Novartis AG; Mitsubishi Pharma Corporation; Yoshitomi Pharmaceutical Industries, Ltd.; Yoshitomi Pharmaceutical Industries, Ltd.; Total Co., Ltd.
  - b. WO 9408943; eidem, US 5604229 (1994, 1997 both to Yoshitomi);
  - c. Originator Mitsubishi Pharma Corporation; Taito
50. DABIGATRAN ETEXILATE MESYLATE
- a. Boehringer Ingelheim GmbH
  - b. WO 9837075; eidem, US 6087380 (1998, 2000 both to Boehringer, Ing.);
  - c. Originator Boehringer Ingelheim
51. LURASIDONE HYDROCHLORIDE
- a. Dainippon Sumitomo Pharma Co., Ltd.; Sumitomo Dainippon Pharma Co Ltd; Sumitomo Dainippon Pharma Co., Ltd.; Sumitomo Pharmaceuticals Company, Limited
  - b. EP 464846; eidem, US 5532372 (1992, 1996 both to Sumitomo).
  - c. Originator Dainippon Sumitomo Pharma
52. CEFTAROLINE FOSAMIL
- a. Forest Laboratories Holdings Limited; Takeda Chemical Industries, Ltd.; Takeda Pharmaceutical Company Limited
  - b. JP 9100283 (1997 to Takeda);
  - c. Originator Takeda
53. TESAMORELIN ACETATE
- a. Applied Research Systems ARS Holding N.V.; Tetra Technologies, Inc.; Theratechnologies, Inc.
  - b. US 5861379 (1996, 1999 both to Theratechnologies).
  - c. Originator Theratechnologies
54. ERIBULIN MESYLATE
- a. Eisai Co., Ltd.; Eisai R&D Management Co., Ltd.
  - b. US 6214865 (2001 to Eisai);
  - c. Originator Eisai Co Ltd; Harvard University

- d. But the drug got a new lease of life in 1998, when Dr. Yoshito Kishi of Harvard developed a completely synthetic halichondrin B and discovered that its cytotoxicity was a function of the macrocyclic lactone C1–C38 moiety [8,12]. Afterwards the synthetic technology was licensed from Harvard to Eisai Research Institute who accomplished the synthesis of the resulting drug, E7389 (NSC 707389) [8,13].  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3954568/>
- e. NCI claims it as part of tech transfer

#### 55. IOFLUPANE I-123

- a. Research Biochemicals Limited Partnership
- b. US 5310912 (1994 to Research Biochemicals);
- c. Originator GE Healthcare
- d. Invented by John L. Neumeyer, researcher at Northeastern at the time  
<https://pubs.acs.org/doi/10.1021/cr050263h>

#### 56. SPINOSAD

- a. DowElanco; Eli Lilly and Company; Johnson & Johnson Consumer Companies, Inc.
- b. No patent
- c. Originator Eli Lilly

#### 57. VILAZODONE HYDROCHLORIDE

- a. Merck Patent Gesellschaft; Merck Patent Gesellschaft mit Beschränkter Haftung; Merck Patentgesellschaft
- b. US 5532241 (1995, 1996 both to Merck Patent GmbH);
- c. Originator Merck KGaA

#### 58. AZILSARTAN KAMEDOXOMIL

- a. Takeda Chemical Industries, Ltd.; Takeda Pharmaceutical Company Limited
- b. US 5243054 (1992, 1993 both to Takeda).
- c. Originator Takeda

#### 59. ROFLUMILAST

- a. AstraZeneca AB; Byk Gulden Lomberg Chemische Fabrik GmbH; Takeda GmbH
- b. US 5712298 (1995, 1998 both to Byk-Gulden).
- c. Originator ALTANA Pharma
- d. Note Altana composes of BYK

#### 60. GADOBUTROL

- a. Schering Aktiengesellschaft
- b. EP 448191 (1991 to Schering AG).
- c. Originator Bayer Schering Pharma

#### 61. VANDETANIB

- a. AstraZeneca AB; AstraZeneca UK Limited
- b. US 7173038 (2001, 2007 both to AstraZeneca);
- c. Originator AstraZeneca

#### 62. GABAPENTIN ENACARBIL

- a. XenoPort, Inc.
- b. US 6818787 (2002, 2004 both to Xenoport);
- c. Originator XenoPort

#### 63. ABIRATERONE ACETATE

- a. British Technology Group, Ltd.; Janssen Oncology, Inc.
  - b. US 5604213 (1993, 1997 both to British Technol. Group);
  - c. Originator The Institute of Cancer Research
- 64. LINAGLIPTIN**
- a. Boehringer Ingelheim International GmbH; Boehringer Ingelheim Pharma GmbH & Co. KG; Probiodrug AG; Trustees of Tufts College; Trustees of Tufts College; 2109617 Ontario Inc.; New England Medical Center Hospitals, Inc.
  - b. US 7407955 (2004, 2008 both to Boehringer Ing.);
  - c. Originator Boehringer Ingelheim
  - d. Priobiodrug is a spinoff: <https://www.medizin.uni-halle.de/fileadmin/Bereichsordner/SonstigeEinrichtungen/Ageing2013/Dokumente Ageing 2017/CVe Demuth 03 2017.pdf>
  - e.
- 65. BOCEPREVIR**
- a. Diatron Corporation; Schering Corporation; Schering Corporation
  - b. US 7012066 (2006 to Schering; Dendreon);
  - c. Originator Schering-Plough
- 66. RILPIVIRINE HYDROCHLORIDE**
- a. AstraZeneca AB; Janssen Pharmaceutica NV
  - b. US 7125879 (2003, 2006 both to Janssen).
  - c. Originator Tibotec Pharmaceuticals
  - d. Tibotec is a spin off <https://pubs-acrs-org.ezp-prod1.hul.harvard.edu/doi/pdf/10.1021/jm040840e>
  - e.
- 67. TELAPREVIR**
- a. Vertex Pharmaceuticals Incorporated
  - b. US 050197299 (2002, 2005 both to Lilly);
  - c. Originator Eli Lilly; Vertex Pharmaceuticals
- 68. FIDAXOMICIN**
- a. Optimer Pharmaceuticals, Inc.
  - b. US 3978211 (1975, 1976 both to Lepetit).
  - c. Originator Optimer Pharmaceuticals
- 69. EZOGABINE**
- a. NA
  - b. US 5384330 (1993, 1995 both to Asta Medica).
  - c. Originator Meda
- 70. INDACATEROL MALEATE**
- a. Novartis AG
  - b. US 6878721 (2000, 2005 both to Novartis).
  - c. Originator Novartis
- 71. RIVAROXABAN**
- a. Bayer HealthCare LLC; Bayer Intellectual Property GmbH; Bayer Schering Pharma Aktiengesellschaft
  - b. US 7157456 (2001, 2007 both to Bayer).
  - c. Originator Bayer; Johnson & Johnson Pharmaceutical Research & Development
- 72. TICAGRELOR**



- a. AstraZeneca AB; AstraZeneca UK Limited
- b. US 6525060 (2000, 2003 both to AstraZeneca);
- c. Originator AstraZeneca

#### 73. VEMURAFENIB

- a. Hoffmann-La Roche Inc.; Hoffmann-LaRoche Inc.; Plexxikon Inc.; Plexxikon Inc.
- b. US 7863288 (2007, 2011 both to Plexxikon).
- c. Originator Plexxikon
- d. Plexxikon: co-founded in 2001 by Joseph Schlessinger of Yale University with Sung-Hou Kim of the University of California, Berkeley.
- e. It uses a proprietary structural biology-based platform called Scaffold-Based Drug Discovery to build a pipeline of products in multiple therapeutic areas.

#### 74. ICATIBANT ACETATE

- a. Hoechst Aktiengesellschaft
- b. US 5648333 (1990, 1997 both to Hoechst).
- c. Originator sanofi-aventis

#### 75. CRIZOTINIB

- a. Agouron Pharmaceuticals Inc; Pfizer Inc.; Pfizer Inc.; Agouron Pharmaceuticals Inc; Sugen, Inc.
- b. US 7858643 (2010 to Agouron).
- c. Originator Pfizer

#### 76. DEFERIPRONE

- a. Apotex Inc
- b. No patent
- c. Originator Royal Free and University College Medical School

#### 77. CLOBAZAM

- a. Na
- b. US 3984398 (1968, 1976 both to Roussel-UCLAF);
- c. Originator OVATION Pharmaceuticals

#### 78. RUXOLITINIB PHOSPHATE

- a. Incyte Holdings Corporation; Incyte Corporation; Incyte Corporation
- b. US 7598257 (2007, 2009 both to Incyte). Enantioselective
- c. Originator Incyte Corporation

#### 79. INGENOL MEBUTATE

- a. LEO Laboratories Limited; NA; Peplin Biotech Pty. Ltd.; Peplin Research Pty Ltd
- b. US 8653133 (2011, 2014, both to LEO Pharma).
- c. Originator National Cancer Institute (USA)
- d. Queensland institute of medical research facilities were used

#### 80. AXITINIB

- a. Agouron Pharmaceuticals Inc; Pfizer Inc.
- b. US 6534524 (2001, 2003 both to Agouron
- c. Originator Pfizer

#### 81. VISMODEGIB

- a. Curis, Inc.; Genentech, Inc.; Curis, Inc.
- b. WO 06028958 (2006 to Genentech; Curis); eidem, US 060063779 (2006).
- c. Originator Curis

#### 82. IVACAFTOR



- a. Vertex Pharmaceuticals, Inc.; Vertex Pharmaceuticals Incorporated
  - b. US 7495103 (2006, 2009 both to Vertex).
  - c. Originator Cystic Fibrosis Foundation Therapeutics; Vertex Pharmaceuticals
83. TAFLUPROST
- a. Santen Pharmaceutical Co., Ltd.; Asahi Glass Company Ltd.
  - b. US 5886035 (1998, 1999 both to Asahi Glass and Santen
  - c. Originator Santen Pharmaceutical
84. LUCINACTANT
- a. The Scripps Research Institute
  - b. No entry
  - c. Originator The Scripps Research Institute
85. PEGINESATIDE ACETATE
- a. Affymax, Inc.
  - b. WO 2004101606 (2004 to Affymax).
  - c. Originator Affymax
86. FLORBETAPIR F-18
- a. The Trustees of the University of Pennsylvania
  - b. US 7687052 (2007, 2010 both to Trustees Univ. Penn.).
  - c. Originator University of Pennsylvania
87. AVANAFIL
- a. Mitsubishi Tanabe Pharma Corporation; Tanabe Seiyaku Co., Ltd.
  - b. US 6656935 (2001, 2003 both to Tanabe Seiyaku).
  - c. Originator Tanabe Seiyaku
88. TALIGLUCERASE ALFA
- a. Protalix Ltd.
  - b. US 080038232 (2008 to Protalix).
  - c. Originator Protalix Biotherapeutics
89. LORCASERIN HYDROCHLORIDE
- a. Arena Pharmaceuticals, Inc.; Hill Dermaceuticals, Inc.
  - b. US 6953787 (2003, 2005 both to Arena);
  - c. Originator Arena Pharmaceuticals
90. MIRABEGRON
- a. Astellas Pharma Inc. ; Yamanouchi Pharmaceutical Co., Ltd.
  - b. US 20090093529 (2004, 2009 both to Astellas)
  - c. Originator Astellas Pharma
91. CITRIC ACID; MAGNESIUM OXIDE; SODIUM PICOSULFATE
- a. Ferring International Center SA
  - b. No entry
  - c. No entry
92. CARFILZOMIB
- a. Cydex Pharmaceuticals, Inc.; Onyx Therapeutics, Inc.; Organ Technologies, Inc.; Proteolix, Inc.
  - b. US 7417042 (2005, 2008 both to Proteolix).
  - c. Originator Proteolix

- d. Proteolix: Founded in 2003 based on technology developed by co-founders Dr. Craig Crews (Yale University) and Dr. Raymond J. Deshaies (California Institute of Technology).

#### 93. ACLIDINIUM BROMIDE

- a. Almirall Prodesfarma, S.A.; Almirall, S.A.; Almirall-Prodesfarma, S.A.; ASTA Medica Aktiengesellschaft; Sofotec GmbH & Co. KG
- b. US 6750226 (2001, 2004 both to Almirall Prodesfarma);
- c. Originator Almirall-Prodesfarma

#### 94. COBICISTAT; ELVITEGRAVIR; EMTRICITABINE; TENOFOVIR DISOPROXIL FUMARATE

- a. Emory University; Gilead Sciences, Inc.; Japan Tobacco, Inc.
- b. Tenofovir: US 5922695 (1998, 1999 both to Gilead). **Elvitegravir**: WO 04046115, US 7176220 (2004, 2007 both to Japan Tobacco). Emtricitabine: WO 9214743 (1992 to Emory University). US 5538975 (1996 to BioChem Pharma); Cobicistate: Preparation: Desai et al., WO 08010921, US 8067449 (2008, 2011, both to Gilead);
- c. Originator Gilead Sciences; Japan Tobacco
- d. **Emory contributed to emtricitabine**

#### 95. LINACLOTIDE

- a. Ironwood Pharmaceutical, Inc.; Ironwood Pharmaceutical, Inc.; Forest Laboratories Holdings Limited; Microbia, Inc.
- b. US 7304036 (2004, 2007 both to Microbia).
- c. Originator Microbia
- d. Microbia was founded in 1998 by postdocs from the lab of Gerald Fink at the Whitehead Institute to commercialize approaches that had been developed in the lab to improve industrial fermentation of fungi, to genetically engineer them to produce secondary metabolites more efficiently or to produce new ones as leads for drug discovery or as products for use in industry, and to identify drug targets in fungi for antifungal drug discovery.

#### 96. ENZALUTAMIDE

- a. The Regents of the University of California
- b. No patent
- c. Originator University of California at Los Angeles; University of Texas M. D. Anderson Cancer Center

#### 97. BOSUTINIB MONOHYDRATE

- a. Wyeth; Wyeth Holdings Corporation; Wyeth LLC
- b. US 6002008 (1998, 1999 both to American Cyanamid).
- c. Originator Wyeth

#### 98. TERIFLUNOMIDE

- a. Aventis Pharmaceuticals Inc.; Hoechst Aktiengesellschaft; Sanofi
- b. US 5494911 (1991, 1996 both to Hoechst).
- c. Originator sanofi-aventis

#### 99. CHOLINE C-11

- a. No patent
- b. No patent
- c. NA
- d. Made by Mayo Clinic

100. REGORAFENIB
  - a. Bayer HealthCare LLC; Bayer Intellectual Property GmbH; Bayer Pharmaceuticals Corporation
  - b. WO 2005009961 (2005 to Bayer)
  - c. Originator Bayer HealthCare
101. PERAMPANEL
  - a. Eisai Co., Ltd.; Eisai R&D Management Co., Ltd.
  - b. WO 2001096308, EP 1300396 (2001, 2009 both to Eisai);
  - c. Originator Eisai Co Ltd
102. OMACETAXINE MEPESUCCINATE
  - a. ChemGenex Pharmaceuticals, Inc.; Ivax International GmbH; Stragen Pharma SA.
  - b. US 7169774 (2007 to Stragen)
  - c. Originator ChemGenex Pharmaceuticals; Stragen Pharma SA
103. TOFACITINIB CITRATE
  - a. Pfizer Inc.
  - b. US 7265221 (2001, 2007 both to Pfizer);
  - c. Originator Pfizer
104. CABOZANTINIB S-MALATE
  - a. Exelixis, Inc.
  - b. US 7579473 (2005, 2009 both to Exelixis);
  - c. Originator Exelixis
  - d. Founded by Spyridon Artavanis-Tsakonas, at Yale at that time, and Corey Goodman and Gerry Rubin who were then at the University of California, Berkeley.
  - e. But later developed candidate. So not clear spin off.
  - f.
105. PONATINIB HYDROCHLORIDE
  - a. NA
  - b. US 20070191376 (2007 to Ariad).
  - c. Originator ARIAD Pharmaceuticals
106. PASIREOTIDE DIASPARTATE
  - a. Novartis AG
  - b. US 7473761 (2002, 2009 both to Novartis);
  - c. Originator Novartis
107. TEDUGLUTIDE RECOMBINANT
  - a. 2109617 Ontario Inc.; Allelix Biopharmaceutical Inc.; NPS Allelix Corp.; NPS Pharmaceuticals, Inc.; Shire-NPS Pharmaceuticals, Inc.
  - b. US 5789379 (1997, 1998 both to Allelix)
  - c. Originator Toronto General Hospital; University of Toronto
108. LOMITAPIDE MESYLATE
  - a. Bristol-Myers Squibb Company; NA; The Trustees of the University of Pennsylvania
  - b. No patent
  - c. Originator Bristol-Myers Squibb
  - d. Note that government contribution not included on patents  
<https://www.keionline.org/27300> . Penn sold parts of royalties for \$55 million

109. APIXABAN
- Bristol-Myers Squibb Company; Pfizer Inc.; Bristol-Myers Squibb Company
  - US 6967208 (2003, 2005 both to Bristol-Myers Squibb);
  - Originator Bristol-Myers Squibb
110. BEDAQUILINE FUMARATE
- Janssen Pharmaceutica NV
  - US 7498343 (2004, 2009 both to Janssen).
  - Originator Johnson & Johnson
111. CROFELEMER
- Napo Pharmaceutcials, Inc.; Salix Pharmaceuticals, Ltd; Napo Pharmaceutcials, Inc.
  - US 5211944 (1992, 1993 both to Shaman Pharmaceuticals).
  - Originator Shaman Pharmaceuticals
112. ALOGLIPTIN BENZOATE
- Probiodrug AG; Takeda Chemical Industries, Ltd.; Takeda Pharmaceutical Company Limited; Trustees of Tufts College; Trustees of Tufts College; 2109617 Ontario Inc.; New England Medical Center Hospitals, Inc.
  - US 050261271 (both 2005 to Takeda).
  - Originator Syrrx Inc
113. MIPOMERSEN SODIUM
- Genzyme Corporation; Isis Pharmaceuticals, Inc.; Isis Pharmaceuticals, Inc.; Novartis AG
  - US 7511131 (2009 to Genzyme).
  - Originator Isis Pharmaceuticals
114. POMALIDOMIDE
- Celanese Corporation
  - US 6335349 (1998, 2002 both to Celgene)
  - Originator Celgene Corporation
115. OSPEMIFENE
- Hormos Medical Corp.; Hormos Medical Ltd.; (Hormos Medical Ltd Oy Tess Diagnostics and Pharmaceuticals Inc);, Quark Pharmaceuticals, Inc.
  - EP 95875 (1986 to Farmos); and use in osteoporosis: M. Degregorio et al., WO 9607402 (1996 to Orion).
  - Originator Hormos Medical
  - Government funding
116. TECHNETIUM TC-99M TILMANOCEPT
- Navidea Biopharmaceuticals, Inc.; The Regents of the University of California
  - No patent
  - Originator University of California, San Diego
117. GADOTERATE MEGLUMINE
- NA
  - DE 3401052, GB 2137612 (both 1984 to Schering).
  - Originator Guerbet
118. DIMETHYL FUMARATE
- Biogen Idec International GmbH; Biogen Idec MA Inc.; Fumapharm AG
  - No patent

- c. Originator Biogen Idec
- 119. CANAGLIFLOZIN
  - a. Mitsubishi Tanabe Pharma Corporation
  - b. WO 2005012326, US 7943788 (2005 to Tanabe, 2011 to Mitsubishi Tanabe).
  - c. Originator Tanabe Seiyaku
- 120. FLUTICASONE FUROATE; VILANTEROL TRIFENATATE
  - a. Glaxo Group Limited; SmithKline Beecham Corporation
  - b. WO 2003024439, EP 1425001 (2003, 2008 both to GSK)
  - c. Originator GlaxoSmithKline; Theravance
- 121. RADIUM RA-223 DICHLORIDE
  - a. Anticancer Therapeutic Inventions AS
  - b. WO 0040275; R. H. Larsen et al., US 6635234 (2000, 2003 both to Anticancer Therapeutic Inventions);
  - c. Originator Algeta
  - d. Norwegian Radium Hospital and the University of Oslo:  
<http://news.cision.com/photocure/r/photocure-subscribes-shares-in-anticancer-therapeutic-inventions-as.c2641666>
- 122. TRAMETINIB DIMETHYL SULFOXIDE
  - a. GlaxoSmithKline; Japan Tobacco, Inc.; Novartis AG
  - b. US 7378423 (2005, 2008 both to Japan Tobacco);
  - c. Originator Japan Tobacco
- 123. DABRAFENIB MESYLATE
  - a. Glaxo SmithKline LLC; GlaxoSmithKline; Japan Tobacco, Inc.; Novartis AG
  - b. US 7994185 (2011 to GSK);
  - c. Originator GlaxoSmithKline
- 124. AFATINIB DIMALEATE
  - a. American Cyanamid Company; Boehringer Ingelheim International GmbH; Boehringer Ingelheim Pharma GmbH & Co. KG
  - b. US 7019012 (2002, 2006 both to Boehringer Ingelheim);
  - c. Originator Boehringer Ingelheim
- 125. DOLUTEGRAVIR SODIUM
  - a. GlaxoSmithKline; Shionogi & Co., Ltd.; Shionogi & Co., Ltd.; VIIV Healthcare Company
  - b. WO 06116764 (2006 to Shionogi);
  - c. Originator Shionogi-GlaxoSmithKline Pharmaceuticals
- 126. VORTIOXETINE HYDROBROMIDE
  - a. H. Lundbeck A/S; H Lundbeck AS
  - b. WO 2003029232, US 7138407 (2003, 2006 both to Lundbeck).
  - c. Originator Lundbeck A/S
- 127. BAZEDOXIFENE ACETATE; ESTROGENS, CONJUGATED
  - a. Wyeth
  - b. US 5998402 (1997, 1999 both to American Home);
  - c. Originator Ligand Pharmaceuticals; Wyeth
  - d. Probably too old to be a spin off
- 128. RIOCIQUAT
  - a. Bayer Aktiengesellschaft; Bayer HealthCare LLC

- b. US 7173037 (2003, 2007 both to Bayer);
  - c. Originator Bayer
129. MACITENTAN
- a. Actelion Pharmaceutical Ltd.
  - b. US 7094781 (2002, 2006 both to Actelion)
  - c. Originator Actelion Pharmaceuticals
130. FLUTEMETAMOL F-18
- a. GE Healthcare Limited; The University of Pittsburgh
  - b. WO 2007020400 (2007 to GE Healthcare).
  - c. Originator University of Pittsburgh
131. ESLICARBAZEPINE ACETATE
- a. BIAL-PORTELA & CA, S.A.; BIAL-PORTELE & CA, S.A.; Portela & C.A., S.A.
  - b. US 5753646 (1997, 1998 both to Portela).
  - c. Originator Bial
132. IBRUTINIB
- a. PHARMACYCLICS LLC; Pharmacyclics, Inc.
  - b. WO 2008039218 (2008 to Pharmacyclics).
  - c. Originator Celera Genomics Group
  - d. Pharmacyclics is a spin off from University of Texas in 1991, but compound created by Celera Genomics and licensed to pharmacyclicsa
133. LULICONAZOLE
- a. Nihon Nohyaku Co., Ltd.; POLA PHARMA INC.
  - b. US 4636519 (1985, 1987 both to Nihon Nohyaku)
  - c. Originator Nihon Nohyaku
134. SIMEPREVIR SODIUM
- a. Medivir AB; Medivir AB; Janssen R&D Ireland; Medivir AB; Janssen Sciences Ireland UC;; Medivir AB; Tibotec Pharmaceuticals Ltd.; NA; Tibotec Pharmaceuticals Ltd.; Medivir AB
  - b. WO 2008092954, EP 2118098 (both 2009 to Tibotec)
  - c. Originator Medivir AB
  - d. Tibotec is a spin off of Rega Institute
  - e. But looks like discovered by Medivir
135. SOFOSBUVIR
- a. Gilead Pharmasset LLC; Pharmasset Inc.
  - b. WO 2010135569 (2010 to Pharmasset));
  - c. Originator Pharmasset
  - d. Pharmasset is a spin off from Emory
136. UMECLIDINIUM BROMIDE; VILANTEROL TRIFENATATE
- a. Glaxo Group Limited
  - b. US 7488827 (2005, 2009 both to GSK). EP 1425001 (2003, 2008 both to GSK);
  - c. Originator GlaxoSmithKline; Theravance
137. DAPAGLIFLOZIN
- a. Alkermes Controlled Therapeutics Inc. II; ALKERMES PHARMA IRELAND LIMITED ; ALKERMES PHARMA IRELAND LIMITED; Amylin Pharmaceuticals, LLC; Alkermes, Inc.

- ; Alkermes, Inc.; Amylin Pharmaceuticals, LLC; Amylin Pharmaceuticals, LLC; AstraZeneca AB
  - ; AstraZeneca Pharmaceuticals LP; Amylin Pharmaceuticals, LLC; Bristol-Myers Squibb Company; Mitsubishi Electric Corporation; TecPharma Licensing AG
- b. US 6515117 (2003 to Bristol-Myers Squibb);
- c. Originator Bristol-Myers Squibb
- 138. TASIMELTEON
  - a. Bristol-Myers Squibb Company; Vanda Pharmaceuticals, Inc.
  - b. US 5856529 (1998, 1999 both to Bristol-Myers Squibb).
  - c. Originator Bristol-Myers Squibb
- 139. DROXIDOPA
  - a. No patent
  - b. US 3920728 (1975 to Hoffmann-La Roche); US 4319040 (1982 to Sumitomo).
  - c. Originator Dainippon Sumitomo Pharma
- 140. MILTEFOSINE
  - a. No patent
  - b. EP 225608; idem, US 4837023 (1987, 1989 both to Max-Planck Ges. Wissensch.).
  - c. Originator Baxter Oncology; Zentaris
- 141. FLORBETABEN F-18
  - a. The Trustees of the University of Pennsylvania
  - b. US 7807135 (2006, 2010, both to Trustees Univ. Penn.);
  - c. Originator Avid Radiopharmaceuticals
- 142. APREMILAST
  - a. Celgene Corporation
  - b. US 7427638 (2003, 2008 both to Celgene).
  - c. Originator Celgene Corporation
- 143. CERITINIB
  - a. Actelion Pharmaceutical Ltd.; AstraZeneca AB; IRM LLC; Novartis AG; Novartis AG; IRM LLC; Rigel Pharmaceuticals, Inc.
  - b. WO 2012082972 (2012 to Novartis). WO 2008073687 (2008 to IRM);
  - c. Originator Novartis
- 144. VORAPAXAR SULFATE
  - a. Schering Corporation
  - b. US 7304078 (2003, 2007 both to Schering Corp.)
  - c. Originator Schering-Plough
- 145. DALBAVANCIN HYDROCHLORIDE
  - a. Vicuron Pharmaceuticals Inc.
  - b. No patent
  - c. Originator Vicuron Pharmaceuticals
- 146. EFINACONAZOLE
  - a. Dow Pharmaceutical Sciences; Kaken Pharmaceutical Co., Ltd.;
  - b. WO 1994026734, US 5620994 (1994, 1997 both to Kaken)
  - c. Originator Kaken Pharmaceutical
- 147. TEDIZOLID PHOSPHATE
  - a. Daewon Pharm. Co., Ltd.; Dong-A Pharmaceuticals Co., Ltd; Trius Therapeutics, Inc.



- b. US 7816379 (2005, 2010 both to DongA)
- c. Originator Dong-A Pharmaceutical
- 148. **BELINOSTAT**
  - a. Topotarget UK Limited
  - b. WO 02030879 (2002 to Prolifix) US 6888027 (2005 to Topotarget).
  - c. Originator TopoTarget
  - d. Collaborations with Three prominent bodies maintain such out-licensing contracts: the National Cancer Institute (USA), the Netherlands Cancer Institute, and Righospitalet (Copenhagen, Denmark).[5]
- 149. **TAVABOROLE**
  - a. Anacor Pharmaceuticals, Inc.
  - b. US 7582621 (2009 to Anacor).
  - c. Originator Anacor Pharmaceuticals
  - d. Anacor is a spin off of Stanford/Penn State. Lucy Shapiro at Stanford University and Stephen Benkovic at Pennsylvania State University
- 150. IDELALISIB
  - a. Gilead Calistoga, LLC.; ICOS;
  - b. WO 2005113556, US 7932260 (2005, 2011 both to ICOS).
  - c. Originator Calistoga Pharmaceuticals
- 151. OLODATEROL HYDROCHLORIDE
  - a. Boehringer Ingelheim International GmbH; Boehringer Ingelheim Pharma GmbH & Co. KG; Boehringer International GmbH; NA
  - b. WO 2005111005, RU 2378262 (2005, 2010 both to Boehringer Ingelheim);
  - c. Originator Boehringer Ingelheim
- 152. EMPAGLIFLOZIN
  - a. Boehringer Ingelheim International GmbH
  - b. WO 2005092877, US 7579449 (2005, 2009 both to Boehringer Ingelheim).
  - c. Originator Boehringer Ingelheim
- 153. ORITAVANCIN DIPHOSPHATE
  - a. Eli Lilly and Company; The Medicines Company; The Medicines Company; AbbVie Inc.
  - b. US 5840684 (1996, 1998 both to Eli Lilly)
  - c. Originator Eli Lilly
- 154. SUVOREXANT
  - a. MERCK SHARP & DOHME CORP.
  - b. US 7951797 (2011 to Merck Sharp & Dohme)
  - c. Originator Merck & Co
- 155. **ELIGLUSTAT TARTRATE**
  - a. Genzyme Corporation; The Regents of the University of Michigan
  - b. US 7196205 (2007 to Regents Univ. Mich.; Genzyme). Enzyme
  - c. Originator University of Michigan
- 156. NALOXEGOL OXALATE
  - a. Nektar Therapeutics AL, Corporation; Nektar Therapeutics UK, Ltd.; Nektar Therapeutics UK, Ltd.; AstraZeneca AB
  - b. US 7786133 (2005, 2010 both to Nektar Therapeutics).
  - c. Originator Nektar Therapeutics



157. NETUPITANT; PALONOSETRON HYDROCHLORIDE
- Helsinn Healthcare SA; Hoffmann-La Roche Inc.; Syntex (U.S.A.) Inc.
  - No entry
  - Originator Helsinn
158. LEDIPASVIR; SOFOSBUVIR
- Gilead Pharmasset LLC; Gilead Sciences, Inc.; Pharmasset Inc.
  - No entry for ledipasvir
  - Originator Gilead Sciences
159. SULFUR HEXAFLUORIDE LIPID-TYPE A MICROSPHERES
- Bracco International BV
  - No patent
  - Originator Bracco
160. PIRFENIDONE
- Intermune, Inc.
  - US 3839346 (1974 to Affiliated Med. Res.)
  - Originator KDL GmbH; Marnac
  - Institute Pasteur a mistaken patent entry
161. NINTEDANIB ESYLATE
- Boehringer Ingelheim GmbH; Boehringer Ingelheim Pharma GmbH & Co. KG;
  - WO 2001027081, US 6762180 (2001, 2004 both to Boehringer Ingelheim);
  - Originator Boehringer Ingelheim
162. FINAFLOXACIN
- Alcon Research, Ltd.; Bayer Aktiengesellschaft
  - US 6133260 (1998, 2000 both to Bayer);
  - Originator Bayer
163. OLAPARIB
- KUDOS PHARMACEUTICALS LIMITED; KUDOS PHARMACEUTICALS LIMITED; Maybridge Limited; KUDOS PHARMACEUTICALS LIMITED; Maybridge PLC; KUDOS PHARMACEUTICALS LIMITED; The Institute of Cancer Research; University Of Sheffield
  - US 7449464 (2004, 2008 both to Kudos Pharm.);
  - Originator KuDOS Pharmaceuticals; University of Pennsylvania
  - Unclear of the University Pennsylvania origin
  - Yorkshire Cancer Research funded the University of Sheffield  
<https://www.sheffield.ac.uk/news/nr/lynparza-breast-cancer-brca-new-therapy-1.757198>
  - Kudos is spinoff of University of Cambridge Prof. Steve Jackson
164. PERAMIVIR
- BioCryst Pharmaceuticals, Inc.
  - US 6562861 (1999, 2003 both to BioCryst Pharm.);
  - Originator BioCryst Pharmaceuticals; University of Alabama
165. DASABUVIR SODIUM ; OMBITASVIR; PARITAPREVIR; RITONAVIR
- Abbott Laboratories; AbbVic Inc.; AbbVie Inc.; Enanta Pharmaceuticals, Inc.; Abbott Laboratories
  - US 8895737 (2012, 2014, both to Abbott); US 8415351 (2009, 2013 to Abbott); WO

- 2010144646 (2011 to Abbot); Degoey et al., US 8691938 (2014 to AbbVie). WO 2010030359, US 8420596 (2011, 2013, both to Enanta and Abbott).
- c. Originator Enanta Pharmaceuticals
166. CEFTOLOZANE SULFATE; TAZOBACTAM SODIUM
- a. Astellas Pharma Inc.; Wakunaga Pharmaceutical Co., Ltd.; Cubist Pharmaceuticals, Inc.; Cymabay Therapeutics, Inc.; MERCK SHARP & DOHME CORP.
- b. WO 04039814 (2004 to Fujisawa; Wakunaga); eidem, US 7129232 (2006 to Astellas; Wakunaga);
- c. Originator Astellas Pharma
167. EDOXABAN TOSYLATE
- a. Daiichi Sankyo Company, Limited
- b. US 7365205 (2003, 2008 both to Daiichi).
- c. Originator Daiichi Sankyo Company
168. PALBOCICLIB
- a. Warner-Lambert Company
- b. US 6936612 (2003, 2005 both to WarnerLambert); WO 2014128588 (2014 to Pfizer).
- c. Originator Onyx Pharmaceuticals; Pfizer
169. LENVATINIB MESYLATE
- a. Eisai Co., Ltd.; Eisai R&D Management Co., Ltd.
- b. US 7253286 (2002, 2007 both to Eisai).
- c. Originator Eisai Co Ltd
170. PANOBINOSTAT LACTATE
- a. Novartis AG
- b. US 6552065 (2002, 2003 both to Novartis).
- c. Originator Novartis
171. AVIBACTAM SODIUM; CEFTAZIDIME
- a. Aventis Pharma S.A.; Forest Laboratories Holdings Limited; Forest Laboratories Holdings Ltd, Aventis Pharma SA; Novoxel
- b. No entry
- c. Originator Novoxel
172. ISAVUCONAZONIUM SULFATE
- a. Basilea Pharmaceutica AG
- b. WO 9945008 (1999 to Hoffmann-LaRoche); eidem, US 6300353 (2001 to Basilea Pharm.);
- c. Originator Basilea Pharmaceutica
173. CHOLIC ACID
- a. NA
- b. No entry
- c. Originator Asklepion Pharmaceuticals
174. IVABRADINE HYDROCHLORIDE
- a. Les Laboratoires Servier
- b. US 5296482 (1993, 1994 both to ADIR).
- c. Originator Servier
175. DEOXYCHOLIC ACID

- a. KYTHERA BIOPHARMACEUTICALS, INC.; The Regents of the University of California; Los Angeles Biomed. Res. Inst. at Harbor UCLA Medical Center; The Regents of the University of California; Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center
  - b. US 2765316 (1956 to Armour).
  - c. Originator Kythera Biopharmaceuticals
  - d. <https://www.prweb.com/releases/2013/11/prweb11322249.htm>
176. ELUXADOLINE
- a. Allergan Holdings Unlimited Company; Forest Tosara Limited; Furiex Pharmaceuticals, Inc.; Janssen Pharmaceutica NV
  - b. US 7741356 (2005, 2010 both to Janssen);
  - c. Originator Janssen Pharmaceutica
177. CANGRELOR
- a. AstraZeneca UK Limited; CHIESI FARMACEUTICI S.p.A.; The Medicines Company
  - b. WO 9418216 (1994 to Fisons); eidem, US 5721219 (1998 to Astra);
  - c. Originator AstraZeneca
178. **IVACAFTOR; LUMACAFTOR**
- a. Vertex Pharmaceuticals Incorporated
  - b. No entry
  - c. Originator Cystic Fibrosis Foundation Therapeutics; Vertex Pharmaceuticals
179. SACUBITRIL; VALSARTAN
- a. Novartis AG; Novartis Pharmaceuticals Corporation
  - b. No entry
  - c. Originator Novartis
180. BREXPIRAZOLE
- a. OTSUKA PHARMACEUTICAL CO., LTD.
  - b. WO 2006112464, EP 1869025 (2006, 2011 both to Otsuka).
  - c. Originator Otsuka Pharmaceutical Development & Commercialization
181. DACLATASVIR DIHYDROCHLORIDE
- a. Bristol-Myers Squibb Company
  - b. US 8329159 (2012 to BMS).
  - c. Originator AmeriCares; Bristol-Myers Squibb
  - d. Unclear how Americares is considered originator
182. SONIDEGIB PHOSPHATE
- a. IRM LLC; Novartis AG
  - b. US 8178563 (2007, 2012, both to IRM)
  - c. Originator Novartis
183. **FLIBANSERIN**
- a. Boehringer Ingelheim GmbH; Sprout Pharmaceuticals, Inc.
  - b. US 5576318 (1993, 1996 both to Boehringer Ingelheim); WO 2003014079, CA 2450093 (2003, 2008 both to Bidachem).
  - c. Originator Boehringer Ingelheim
  - d. Compound was initially discovered as antidepressant
184. ROLAPITANT HYDROCHLORIDE
- a. Opko Health, Inc.; Schering Corporation
  - b. US 7049320 (2003, 2006, both to Schering).

- c. Originator Schering-Plough
- 185. URIDINE TRIACETATE
  - a. Pro-Neuron, Inc.
  - b. No patent
  - c. Originator Wellstat Therapeutics Corporation
  - d. Pro-neuron – scientific founder is Michal Schwarts (Weizmann Institute of Science) in Israel in 1996, but may not be related.
- 186. CARIPRAZINE HYDROCHLORIDE
  - a. Richter Gedeon Nyrt.; Richter Gedeon Vegyeszeti Gyar Rt.
  - b. US 7737142 (2005, 2010, both to Richter Gedeon).
  - c. Originator Gedeon Richter
- 187. TIPIRACIL HYDROCHLORIDE; TRIFLURIDINE
  - a. Taiho Pharmaceutical Co., Ltd.
  - b. US 5744475 (1996, 1998, both to Taiho);
  - c. Originator Taiho Pharmaceutical
- 188. INSULIN DEGLUDEC
  - a. Novo Nordisk A/S
  - b. No entry
  - c. Originator Novo Nordisk
- 189. ARIPIPRAZOLE LAUROXIL
  - a. ALKERMES PHARMA IRELAND LIMITED
  - b. US 8431576 (2010, 2013, both to Alkermes).
  - c. Originator Alkermes
- 190. PATIROMER SORBITEX CALCIUM
  - a. Relypsa Inc; IYPSA
  - b. US 8337824 (2010, 2012 both to Relypsa
  - c. Originator Relypsa
- 191. TRABECTEDIN
  - a. Pharma Mar, S.A., Sociedad Unipersonal
  - b. No entry
  - c. Originator University of Illinois
  - d. University of Illinois <https://www.thepharmaletter.com/article/zeltia-agrees-to-pay-for-yondelis-patent>
- 192. COBICISTAT; ELVITEGRAVIR; EMTRICITABINE; TENOFOVIR ALAFENAMIDE FUMARATE
  - a. Brother Kogyo Kabushiki Kaisha; Emory University; Gilead Sciences, Inc.; Japan Tobacco, Inc.; NA
  - b. No entry for TAF
  - c. Originator Gilead Sciences
  - d. Emory developed emtricitabine?
- 193. COBIMETINIB FUMARATE
  - a. Exelixis, Inc.
  - b. US 7803839 (2007, 2010, both to Exelixis);
  - c. Originator Exelixis
- 194. OSIMERTINIB MESYLATE
  - a. AstraZeneca AB

- b. US 8946235 (2013, 2015 both to AstraZeneca);
- c. Originator AstraZeneca
- 195. IXAZOMIB CITRATE**
  - a. Cephalon, Inc.; Millennium Pharmaceuticals, Inc.; NA
  - b. US 8859504 (2009, 2014 both to Millennium
  - c. Originator Millennium Pharmaceuticals
  - d. Millennium pharmaceuticals is spin off of MIT in 1993, but has been a long time so likely independently developed
- 196. ALECTINIB HYDROCHLORIDE
  - a. Chugai Seiyaku Kabushiki Kaisha
  - b. US 9126931 (2010, 2015 both to Chugai)
  - c. Originator Chugai Pharmaceutical
- 197. SUGAMMADEX SODIUM
  - a. Akzo Nobel N.V.; MERCK SHARP & DOHME CORP.; Organon N.V.; Taiwan Semiconductor Manufacturing Company, Ltd.
  - b. US 6670340 (2001, 2003 both to Akzo Nobel)
  - c. Originator Organon
- 198. SELEXIPAG
  - a. Actelion Pharmaceutical Ltd.; Nippon Shinyaku Co. Ltd.
  - b. US 7205302 (2002, 2007 both to Nippon Shinyaku)
  - c. Originator Nippon Shinyaku
- 199. LESINURAD
  - a. Ardea Biosciences Inc.
  - b. US 7947721 (2006 to Valeant, 2011 to Ardea Biosciences); WO 2015075561 (2015 to Crystal Pharmatech).
  - c. Originator Ardea Biosciences
- 200. ELBASVIR; GRAZOPREVIR
  - a. Istituto di Ricerche di Biologia Molecolare P. Angeletti SpA; MERCK SHARP & DOHME CORP.; MERCK SHARP & DOHME CORP.
  - b. US 8871759 (2010, 2014, both to MSD); US 7973040 (2010, 2011, both to MSD)
  - c. Originator Merck & Co
- 201. BRIVARACETAM
  - a. UCB Pharma S.A.; UCB, S.A.
  - b. US 6911461 (2001, 2005 both to UCB);
  - c. Originator UCB
- 202. DEFIBROTIDE SODIUM
  - a. NA
  - b. US 3899481 (1972, 1975 both to Crinos).
  - c. Originator Gentium
  - d. Italian biotech company
- 203. VENETOCLAX**
  - a. AbbVie Inc.; Genentech, Inc.; AbbVie Inc.; The Walter and Eliza Hall Institute of Medical Research
  - b. US 8546399 (2011 to Abbott, 2013 to AbbVie).
  - c. Originator Abbott Laboratories; Genentech; Walter and Eliza Hall Institute of Medical Research

204. PIMAVANSERIN TARTRATE
- Acadia Pharmaceuticals Inc.; Ipsen Pharma S.A.S.; Societe de Conseils de Recherches et d'Applications Scientifiques SCRAS
  - US 7732615 (2006, 2010, both to Acadia Pharmaceuticals).
  - Originator ACADIA Pharmaceuticals
205. FLUCICLOVINE F-18
- Emory University; Nihon Medi-Physics Co., Ltd.
  - No entry
  - Originator Emory University
206. OBETICHOLIC ACID
- Intercept Pharmaceuticals, Inc.
  - US 7138390 (2002, 2006 both to Intercept Pharmaceuticals);
  - Originator GlaxoSmithKline; Universita degli Studi di Perugia
  - Discovery from joint collaboration between GSK and University of Perugia scientist in 2001.
207. GALLIUM DOTATATE GA-68
- NA
  - No entry specific for dotatate
  - Originator Advanced Accelerator Applications
208. SOFOSBUVIR; VELPATASVIR
- Gilead Pharmasset LLC; Gilead Sciences, Inc.; PharmaJet Inc.
  - US 9156823 (2012, 2015 both to Gilead).
  - Originator Gilead Sciences
  - Pharmasset is spin of emory (Sofosbuvir)
209. LIFITEGRAST
- SARcode Bioscience Inc.; Siecor Corporation; Sunesis Pharmaceuticals, Inc.
  - US 8084047 (2006, 2011 both to SARcode Bioscience
  - Originator Sunesis Pharmaceuticals
  - Sunesis founded in 1998, by Jim Wells, James A Wells both at UCSF.
210. LIXISENATIDE
- Sanofi-Aventis Deutschland GmbH; Zealand Pharma A/S
  - WO 0104156 (2001 to Zealand).
  - Originator Zealand Pharma
211. ETEPLIRSEN
- Academisch Ziekenhuis Leiden; BioMarin Technologies B.V.; Sarepta Therapeutics, Inc.; The University of Western Australia
  - No entry
  - Originator AVI BioPharma; Ercole Biotech
212. CRISABOROLE
- Anacor Pharmaceuticals, Inc.
  - US 8039451 (2006, 2011 to Anacor Pharmaceuticals);
  - Originator Anacor Pharmaceuticals
213. RUCAPARIB CAMSYLATE
- Agouron Pharmaceuticals Inc; Cancer Research Technology Limited; Pfizer; KUDOS PHARMACEUTICALS LIMITED; The Institute of Cancer Research; KUDOS PHARMACEUTICALS LIMITED; The Institute of Cancer Research; Royal Cancer

- Hospital; Pfizer Inc.; Pfizer Inc.; Cancer Research Technology Limited; University Of Sheffield
- b. US 6495541 (2000, 2002 to Agouron); WO 2006033003 (2006 to Pfizer and Cancer Research Technology) [US7323562B2], US 7323562 (2008 to Agouron and Cancer Research Technology).
  - c. Originator Cancer Research UK
- 214. NUSINERSEN SODIUM**
- a. Biogen MA Inc.; Cold Spring Harbor Laboratory; Cold Spring Harbor Laboratory; Isis Pharmaceuticals, Inc.; Isis Pharmaceuticals, Inc.; University of Massachusetts
  - b. WO 2010148249, US 8980853 (2010 to Isis Pharmaceuticals, Genzyme and Cold Spring Harbor Laboratory, 2015 to Isis Pharmaceuticals and Cold Spring Harbor Laboratory).
  - c. Originator Callisto Pharmaceuticals
215. PLECANATIDE
- a. Callisto Pharmaceuticals; Synergy Pharmaceuticals, Inc.
  - b. US 7041786 ((2002, 2006 both to Synergy Pharmaceuticals).
  - c. Originator Callisto Pharmaceuticals
- 216. ETELCALCETIDE**
- a. Amgen Inc.; KAI Pharmaceuticals, Inc.
  - b. US 8377880 (2011, 2013 both to Kai Pharmaceuticals);
  - c. Originator KAI Pharmaceuticals
  - d. Kai Pharmaceuticals is spinoff of Stanford University, but not clear drug is related
217. DEFLAZACORT
- a. NA
  - b. US 3436389 (1966, 1967, 1969 all to Lepetit);
  - c. Originator Marathon Pharmaceuticals
- 218. TELOTRISTAT ETIPRATE**
- a. Lexicon Pharmaceuticals, Inc.
  - b. US 8193204 (2009, 2012, both to Lexicon Pharmaceuticals).
  - c. Originator Lexicon Pharmaceuticals
  - d. Founded in September 1995 as a biotech venture of Baylor College of Medicine (originally as Lexicon Genetics Incorporated). Though likely has been too much time.
- 219. RIBOCICLIB SUCCINATE**
- a. ASTEX THERAPEUTICS LTD; Novartis AG; Novartis AG
  - b. 8415355 (2010, 2013 both to Novartis and Astex).
  - c. Originator Astex Therapeutics
  - d. Founded in 1999, by University of Cambridge researchers Sir Tom Blundell Chris Abell:
- 220. SAFINAMIDE MESYLATE**
- a. Newron Pharmaceuticals, S.p.A.
  - b. US 5236957 (1990, 1993 both to Farmitalia);
  - c. Originator Pfizer
  - d. Received government funding from Italy
221. NALDEMEDINE TOSYLATE



- a. Shionogi & Co., Ltd.
  - b. US 8084460 (2006, 2011 both to Shionogi)
  - c. Originator Shionogi
222. NIRAPARIB TOSYLATE
- a. Istituto di Ricerche di Biologia Molecolare P. Angeletti SpA; MERCK SHARP & DOHME CORP.
  - b. US 8436185 (both 2009 to Merck Sharp & Dohme).
  - c. Originator Merck & Co
223. DEUTETRABENAZINE
- a. AUSPEX PHARMACEUTICALS, INC.
  - b. No entry
  - c. Originator Auspex Pharmaceuticals
224. VALBENAZINE TOSYLATE
- a. Neurocrine Biosciences, Inc.
  - b. US 8039627 (2008, 2011, both to Neurocrine Biosciences).
  - c. Originator Neurocrine Biosciences
  - d. Spin off; academic founders were Wylie Vale of the Salk Institute for Biological Studies and Lawrence Steinman of Stanford University. But in 1992, so likely a long way out.
225. BRIGATINIB
- a. ARIAD Pharmaceuticals Inc
  - b. No entry
  - c. Originator ARIAD Pharmaceuticals
226. MIDOSTAURIN
- a. Novartis AG; Dana-Farber Cancer Institute, Inc.
  - b. US 5093330 (1988, 1992 both to Ciba-Geigy);
  - c. Originator Novartis
227. ABALOPARATIDE
- a. Radius Health, Inc.; Ipsen Pharma S.A.S.
  - b. US 8148333 (2009, 2012 to Radius Health and Ipsen Pharma); and clinical study: Dey et al., WO 2009137093, US 7803770 (2009, 2010 to Radius Health and Ipsen Pharma).
  - c. Originator 3M Drug Delivery Systems; Biomeasure Inc; Ipsen
228. EDARAVONE
- a. Mitsubishi Pharma Corporation
  - b. No patent
  - c. Originator Mitsubishi Pharma Corporation
229. DELAFLOXACIN MEGLUMINE
- a. Abbott Laboratories; AbbVie Inc.; Melinta Therapeutics, Inc.; Rib-X Pharmaceuticals, Inc.
  - b. US 5998436 (1997, 1999 both to Wakunaga).
  - c. Originator Wakunaga Pharmaceutical
  - d. Rib-X is a spin off from Yale, but acquired product from Wakunaga
  - e. Rib-X platform takes advantage of Tomas Steitz' work.
230. BETRIXABAN



- a. COR Therapeutics, Inc.; Millennium Pharmaceuticals, Inc.; Millennium Pharmaceuticals, Inc.; Portola Pharmaceuticals, Inc.
  - b. US 6376515 (2001, 2002 to COR Therapeutics, Millennium Pharmaceuticals);
  - c. Originator Millennium Pharmaceuticals
  - d. Millennium is spin off from MIT in 1993, but due to time likely not
231. NERATINIB MALEATE
- a. American Cyanamid Company; Wyeth; Wyeth LLC
  - b. US 7399865 (2005, 2008 both to Wyeth);
  - c. Originator Wyeth
232. SOFOSBUVIR; VELPATASVIR; VOXILAPREVIR
- a. Gilead Pharmasset LLC; Gilead Sciences, Inc.; NA; Pharmasset Inc.
  - b. US 9655944 (2014, 2017, both to Gilead).
  - c. Originator Gilead Sciences
  - d. Sofosbuvir – Pharmasset, spin off of Emory
233. ENASIDENIB MESYLATE
- a. AGIOS PHARMACEUTICALS, INC
  - b. No entry
  - c. Originator Agios Pharmaceuticals
234. GLECAPREVIR; PIBRENTASVIR
- a. AbbVie Inc.; Enanta Pharmaceuticals, Inc.
  - b. US 8648037 (2012, 2014, both to Enanta Pharm); US 9321807 (2015, 2016, both to AbbVie). US 8937150 (2012 to Abbott, 2015 to AbbVie);
  - c. Originator AbbVie; Enanta Pharmaceuticals
235. BENZNIDAZOLE
- a. NA
  - b. US 3679698 (1966, 1972 both to HoffmannLa Roche).
  - c. Originator Chemo Group
  - d. Drugs for Neglected Diseases Initiative Foundation provided development support to get the drug approved in the US.
236. MEROPENEM; VABORBACTAM
- a. Rempex Pharmaceuticals, Inc.
  - b. US 8680136 (2012, 2014 both to Rempex Pharmaceuticals);
  - c. Originator Rempex Pharmaceuticals
237. COPANLISIB DIHYDROCHLORIDE
- a. Bayer Intellectual Property GmbH; Bayer Pharmaceuticals Corporation
  - b. US 8466283 (2008 to Bayer Schering Pharma, 2013 to Bayer);
  - c. Originator Bayer Schering Pharma
238. SECNIDAZOLE
- a. NA
  - b. FR M3270 (1965 to RhônePoulenc),
  - c. Originator Symbiomix Therapeutics
239. ABEMACICLIB
- a. Eli Lilly and Company
  - b. No entry
  - c. Originator Eli Lilly
240. ACALABRUTINIB

- a. MERCK SHARP & DOHME CORP.; Acerta Pharma BV
  - b. US 6750226 (2001, 2004 both to Almirall Prodesfarma); WO 08009397 (2008 to Almirall).
  - c. Originator Acerta Pharma
241. LATANOPROSTENE BUNOD
- a. Nicox S.A.
  - b. No entry
  - c. Originator NicOx
242. LETERMOVIR
- a. AiCuris GmbH & Co. KG; Bayer HealthCare LLC
  - b. No entry
  - c. Originator Bayer
243. SEMAGLUTIDE
- a. Novo Nordisk A/S
  - b. No entry
  - c. Originator Novo Nordisk
244. OZENOXACIN
- a. Ferrer Internacional S.A.; Toyama Chemical Co., Ltd.
  - b. WO 1999051588, US 6335447 (1999, 2002 both to Toyama Chemical Co.).
  - c. Originator Toyama Chemical
245. NETARSUDIL DIMESYLATE
- a. Aerie Pharmaceuticals, Inc.
  - b. No entry
  - c. Originator Duke University Medical Center
  - d. Aerie is a spin off of Duke
246. ERTUGLIFLOZIN
- a. Pfizer Inc.
  - b. No entry
247. MACIMORELIN ACETATE
- a. AEterna Zentaris GmbH; Zentaris AG
  - b. No entry
  - c. Originator AEterna Zentaris Inc
248. ANGIOTENSIN II ACETATE
- a. The George Washington University, a Congressionally Not-for-Profit Corporation
  - b. No patent
  - c. Originator La Jolla Pharmaceutical Company

## Appendix: R Code

### Patent Data EOB Merge.R

```
#Txt files for patents first converted to csv
Folder = "C:/Users/Rahul/OneDrive - Harvard University/HMS/SIM/EOB/Data"
setwd(Folder)
files = list.files(Folder,pattern="*.txt")

#Combining Files
Patents = NULL
Patents2 = NULL
for(i in 1:6){
  df = read.table(files[i],sep = "~",header=T,stringsAsFactors=F)
  Patents = rbind(Patents,df)
}

for(i in 7:11){
  df = read.table(files[i],sep = "~",header=T,stringsAsFactors=F)
  Patents2 = rbind(Patents2,df)
}

#Standardizing Name and Columns
names(Patents)[names(Patents)=="drug_substance_flag"] <- "Drug_Substance_Flag"
names(Patents)[names(Patents)=="drug_product_flag"] <- "Drug_Product_Flag"

Patents12 = rbind(Patents,Patents2)
Patents12$Submission_Date <- NA

Patents3 = read.table(files[12],sep = "~",header=T,stringsAsFactors=F)

#Raw Combined Data
Patents_ALL_2009_2017 = rbind(Patents12,Patents3)

#Unique Listings
Patents_ALL_2009_2017.unique <- unique(Patents_ALL_2009_2017[, 1:10 ])

#Pediatric Exclusivity
Patents_ALL_2009_2017.unique$Ped <- as.integer(grepl(pattern = "*PED",
x=Patents_ALL_2009_2017.unique$Patent_No))
Patents_ALL_2009_2017.unique$Patent_No_Clean <- gsub("[^0-
9]", "",x=Patents_ALL_2009_2017.unique$Patent_No)

#Duplicate Patent Listings
```

```
Patents_ALL_2009_2017.unique$Duplicate <-
duplicated(Patents_ALL_2009_2017.unique$Patent_No_Clean)
Patents_ALL_2009_2017.unique_uniq <-
Patents_ALL_2009_2017.unique[which(Patents_ALL_2009_2017.unique$Duplicate==FALS
E),]
```

```
#Fixing Date
```

```
Patents_ALL_2009_2017.unique_uniq$Patent_Expire_Date_Text <-
as.Date(Patents_ALL_2009_2017.unique_uniq$Patent_Expire_Date_Text, "%b %d, %Y")
```

```
#Export Data
```

```
write.csv(Patents_ALL_2009_2017,file = "EOB Data Files Patent 2009-2017 - All
Combinations.csv")
write.csv(Patents_ALL_2009_2017.unique, file = "EOB Data Files Patent 2009-2017 -
Unique Entries.csv")
write.csv(Patents_ALL_2009_2017.unique_uniq, file = "EOB Data Files Patent 2009-2017 -
Unique Patents.csv")
```

### **Obtaining Patent Metadata.R**

```
#install.packages("devtools")
#devtools::install_github("ropensci/patentsview")
#install.packages("patentsview")
require(patentsview)
require(base)
```

```
##Importing data
```

```
Products <- read.csv("C:/Users/Rahul/OneDrive - Harvard University/HMS/SIM/Publically
Funded Drugs/EOBZIP_2017_12/products.csv")
Patents <- read.csv("C:/Users/Rahul/OneDrive - Harvard University/HMS/SIM/Publically
Funded Drugs/EOBZIP_2017_12/patent.csv")
Exculsivity <- read.csv("C:/Users/Rahul/OneDrive - Harvard
University/HMS/SIM/Publically Funded Drugs/EOBZIP_2017_12/exclusivity.csv")
```

```
##Fixing Heading Names
```

```
names(Products)[names(Products)=="i..Ingredient"] <- "Ingredient"
names(Patents)[names(Patents)=="i..Appl_Type"] <- "Appl_Type"
names(Exculsivity)[names(Exculsivity)=="i..Appl_Type"] <- "Appl_Type"
```

```
#Pediatric Exclusivity
```

```
Patents$Ped <- as.integer(grepl(pattern = "*PED", x=Patents$Patent_No))
Patents$Patent_No_Clean <- gsub("[^0-9]", "",x=Patents$Patent_No)
```

```
#Duplicate Patent Listings
```

```
Patents$Duplicate <- duplicated(Patents$Patent_No_Clean)
```

```
#Including NDAs Only
```

```

Products_N <- Products[which(Products$Appl_Type=='N'),]

#Dropping duplicate approvals
Products_N <- Products_N[order(Products_N$Appl_No, Products_N$Product_No),]
Products_N$Duplicate <- duplicated(Products_N$Appl_No)
Products_N_uniq <- Products_N[which(Products_N$Duplicate==FALSE),]

#Combing Datasets
Combined <- merge(Products_N_uniq, Patents, by=c("Appl_No"), all=TRUE)
View(Combined)

#Unique Patent List
Patents_uniq <- Patents[which(Patents$Duplicate==FALSE),]

#Unique Exclusivity List

##Getting Patent Data
PatentList <- c()
PatentList <- Patents_uniq$Patent_No_Clean

#Determining fields

#f <- get_fields("patents") #To Get all fields

#Application Data
App<-c("app_country", "app_date", "app_number", "app_type")

#Patents Data
Pat <- c("patent_average_processing_time", "patent_date",
"patent_firstnamed_assignee_city", "patent_firstnamed_assignee_country",
"patent_firstnamed_assignee_id", "patent_firstnamed_assignee_latitude",
"patent_firstnamed_assignee_location_id", "patent_firstnamed_assignee_longitude",
"patent_firstnamed_assignee_state", "patent_firstnamed_inventor_city",
"patent_firstnamed_inventor_country", "patent_firstnamed_inventor_id",
"patent_firstnamed_inventor_latitude", "patent_firstnamed_inventor_location_id",
"patent_firstnamed_inventor_longitude", "patent_firstnamed_inventor_state", "patent_id",
"patent_kind", "patent_num_cited_by_us_patents", "patent_num_claims",
"patent_num_combined_citations", "patent_num_foreign_citations",
"patent_num_us_application_citations", "patent_num_us_patent_citations",
"patent_number", "patent_processing_time", "patent_title", "patent_type", "patent_year")

#Inventors Data
Inventor <- c("inventor_city", "inventor_country", "inventor_county",
"inventor_county_fips", "inventor_first_name", "inventor_first_seen_date", "inventor_id",
"inventor_last_name", "inventor_last_seen_date", "inventor_lastknown_city",

```

```
"inventor_lastknown_country", "inventor_lastknown_latitude",  
"inventor_lastknown_location_id", "inventor_lastknown_longitude",  
"inventor_lastknown_state", "inventor_latitude", "inventor_location_id",  
"inventor_longitude", "inventor_sequence", "inventor_state", "inventor_state_fips",  
"inventor_total_num_patents")
```

#### #Assignee Data

```
Assignee <- c("assignee_city", "assignee_country", "assignee_county",  
"assignee_county_fips", "assignee_first_name", "assignee_first_seen_date", "assignee_id",  
"assignee_last_name", "assignee_last_seen_date", "assignee_lastknown_city",  
"assignee_lastknown_country", "assignee_lastknown_latitude",  
"assignee_lastknown_location_id", "assignee_lastknown_longitude",  
"assignee_lastknown_state", "assignee_latitude", "assignee_location_id",  
"assignee_longitude", "assignee_organization", "assignee_sequence", "assignee_state",  
"assignee_state_fips", "assignee_total_num_inventors", "assignee_total_num_patents",  
"assignee_type")
```

#### #Gov Interest

```
Gov <- c("govint_contract_award_number", "govint_org_id", "govint_org_level_one",  
"govint_org_level_three", "govint_org_level_two", "govint_org_name",  
"govint_raw_statement")
```

#### #Citation

```
Citations <- c("appcit_app_number", "appcit_category", "appcit_date", "appcit_sequence",  
"cited_patent_category", "cited_patent_date", "cited_patent_kind", "cited_patent_number",  
"cited_patent_sequence", "cited_patent_title", "citedby_patent_category",  
"citedby_patent_date", "citedby_patent_kind", "citedby_patent_number",  
"citedby_patent_title")
```

#### #CPCs

```
CPC <- c("cpc_category", "cpc_first_seen_date", "cpc_group_id", "cpc_group_title",  
"cpc_last_seen_date", "cpc_section_id", "cpc_sequence", "cpc_subgroup_id",  
"cpc_subgroup_title", "cpc_subsection_id", "cpc_subsection_title",  
"cpc_total_num_assignees", "cpc_total_num_inventors", "cpc_total_num_patents")
```

#### #USPCs

```
USPC <- c("uspc_first_seen_date", "uspc_last_seen_date", "uspc_mainclass_id",  
"uspc_mainclass_title", "uspc_sequence", "uspc_subclass_id", "uspc_subclass_title",  
"uspc_total_num_assignees", "uspc_total_num_inventors", "uspc_total_num_patents")
```

#### #NBER

```
NBER <- c("nber_category_title", "nber_first_seen_date", "nber_last_seen_date",  
"nber_subcategory_id", "nber_subcategory_title", "nber_total_num_assignees",  
"nber_total_num_inventors", "nber_total_num_patents")
```

#### #Lawyer

```

Lawyer <- c("lawyer_first_name", "lawyer_first_seen_date", "lawyer_id",
"lawyer_last_name", "lawyer_last_seen_date", "lawyer_organization", "lawyer_sequence",
"lawyer_total_num_assignees", "lawyer_total_num_inventors", "lawyer_total_num_patents")

#Examiner
Examiner <- c("examiner_first_name", "examiner_group", "examiner_id",
"examiner_last_name", "examiner_role")

#Foreign Priority
Foreign <- c("forprior_country", "forprior_date", "forprior_docnumber", "forprior_kind",
"forprior_sequence")

f <- c(App, Pat, Inventor, Assignee, Gov, Citations)
Scraped_Data = as.data.frame(NULL)
PatentList_Num <- as.numeric(PatentList)
for (i in 758:800){
  data<-search_pv(qry_funs$eq(patent_number=PatentList[i]),fields =
f,endpoint="patents")
  if (!is.null(data$data$patents)){
    v <- as.data.frame(data$data$patents)
    v0 <- v[,1:29]
    v0a <- t(apply(v0, 2, paste, collapse="; "))
    v1 <- as.data.frame(data$data$patents$assignees)
    v1a <- t(apply(v1, 2, paste, collapse="; "))
    v2 <- as.data.frame(data$data$patents$inventors)
    v2a <-t(apply(v2, 2, paste, collapse="; "))
    v3 <- as.data.frame(data$data$patents$applications)
    v3a <- t(apply(v3, 2, paste, collapse="; "))
    v4 <- as.data.frame(data$data$patents$application_citations)
    v4a <- t(apply(v4, 2, paste, collapse="; "))
    v5 <- as.data.frame(data$data$patents$cited_patents)
    v5a <- t(apply(v5,2,paste,collapse="; "))
    v6 <- as.data.frame(data$data$patents$citedby_patents)
    v6a <- t(apply(v6,2,paste,collapse="; "))
    v7 <- as.data.frame(data$data$patents$gov_interests)
    v7a <- t(apply(v7, 2, paste, collapse="; "))
    v_comb <- cbind(PatentList[i],v0a,v1a,v2a,v3a,v4a,v5a,v6a,v7a)
    Scraped_Data <- rbind(Scraped_Data,v_comb)
  }
  else {
    v_comb <- as.data.frame(cbind(PatentList[i],t(rep(NA,105))))
    names(v_comb)<-names(Scraped_Data)
    Scraped_Data <- rbind(Scraped_Data,v_comb)
  }
  print(i)
}

```

```

#write.csv(Scraped_Data,file = "C:/Users/Rahul/OneDrive - Harvard
University/HMS/SIM/Publically Funded Drugs/Scraped Data799-799.csv")
Scraped_Data_Combined <- read.csv("C:/Users/Rahul/OneDrive - Harvard
University/HMS/SIM/Publically Funded Drugs/EOBZIP_2017_12/Scraped Data
Combined.csv",stringsAsFactors = FALSE)

#Exclusivity Unique
Patents$Exclusivity <- duplicated(Exculsivity$Appl_No)
Exclusivity_uniq <- Exculsivity[!(duplicated(Exculsivity[c("Appl_No","Exclusivity_Code"))]),
]

#Combining Datasets
Comb_prod_pat <- merge(Products_N_uniq, Patents_uniq, by=c("Appl_No"), all=TRUE)
Comb_all <- merge(Comb_prod_pat, Exclusivity_uniq, by=c("Appl_No"), all=TRUE)

#Drug Approval Since 1982
Comb_all_1982 <- Comb_all[which(Comb_all$Approval_Date!="Approved Prior to Jan 1,
1982"),]
Comb_all_1982$Approval_Date <- as.Date(Comb_all_1982$Approval_Date, "%d-%b-%y")
Comb_prod_pat_1982 <-
Comb_prod_pat[which(Comb_prod_pat$Approval_Date!="Approved Prior to Jan 1, 1982"),]
Comb_prod_pat_1982$Approval_Date <- as.Date(Comb_prod_pat_1982$Approval_Date,
"%d-%b-%y")

View(Comb_all_1982[which(Comb_all_1982$Approval_Date>=as.Date("01-Jan-07","%d-
%b-%y")),])
View(Comb_prod_pat_1982[which(Comb_prod_pat_1982$Approval_Date>=as.Date("01-
Jan-07","%d-%b-%y")),])
#3335

#Merge Scraped Patent Data
Comb_prod_pat_scraped <- merge(Comb_prod_pat, Scraped_Data_Combined,
by.x="Patent_No_Clean", by.y="x", all=TRUE)

###New part - adding in the patents without metadata
#install.packages("patentsview")
require(patentsview)
require(base)
#Txt files for patents first merged using excel.
Folder = "C:/Users/rkn3/Dropbox (Partners HealthCare)/DOPE/4. EOB"
setwd(Folder)

```



```

Patents_2001_2018 = read.csv("Combined Patents 2001-
2018.csv",header=T,stringsAsFactors = F)

#Pediatric Exclusivity
Patents_2001_2018$Ped <- as.integer(grepl(pattern = "*PED",
x=Patents_2001_2018$Patent_No))
Patents_2001_2018$Patent_No_Clean <- gsub("[^0-
9]", "",x=Patents_2001_2018$Patent_No)

#Duplicate Patent Listings
Patents_2001_2018$Duplicate <- duplicated(Patents_2001_2018$Patent_No_Clean)
Patents_2001_2018_unique <-
Patents_2001_2018[which(Patents_2001_2018$Duplicate==FALSE),]

#Note that pediatric information is not accurate for Patents_2001_2018_unique

#Merging Scrapped patent data
Folder = "C:/Users/rkn3/Dropbox (Partners HealthCare)/DOPE/5. Patent Data"
setwd(Folder)
Scrapped_patents = read.csv("Scraped Data Combined.csv",header=T,stringsAsFactors = F)
Reissued = read.csv("Reissued.csv",header=T,stringsAsFactors = F)
merged_patents <- merge(Patents_2001_2018_unique, Scrapped_patents,
by.x="Patent_No_Clean", by.y="x", all=TRUE)
merged_patents$needPatentData <- is.na(merged_patents$patent_date)
merged_patents$needPatentData_prevFail <-
is.na(merged_patents$patent_date)&(!is.na(merged_patents$X))

PatentList_New <-
merged_patents$Patent_No_Clean[merged_patents$needPatentData==TRUE &
merged_patents$needPatentData_prevFail==FALSE]

PatentList_OldFail <-
merged_patents$Patent_No_Clean[merged_patents$needPatentData==TRUE &
merged_patents$needPatentData_prevFail==TRUE]

PatentList_Reissued <- Reissued$Patent

#New Patents
#Determining fields

#f <- get_fields("patents") #To Get all fields

App<-c("app_country", "app_date", "app_number", "app_type")
Pat <- c("patent_average_processing_time", "patent_date",
"patent_firstnamed_assignee_city", "patent_firstnamed_assignee_country",
"patent_firstnamed_assignee_id", "patent_firstnamed_assignee_latitude",

```

```

"patent_firstnamed_assignee_location_id", "patent_firstnamed_assignee_longitude",
"patent_firstnamed_assignee_state", "patent_firstnamed_inventor_city",
"patent_firstnamed_inventor_country", "patent_firstnamed_inventor_id",
"patent_firstnamed_inventor_latitude", "patent_firstnamed_inventor_location_id",
"patent_firstnamed_inventor_longitude", "patent_firstnamed_inventor_state", "patent_id",
"patent_kind", "patent_num_cited_by_us_patents", "patent_num_claims",
"patent_num_combined_citations", "patent_num_foreign_citations",
"patent_num_us_application_citations", "patent_num_us_patent_citations",
"patent_number", "patent_processing_time", "patent_title", "patent_type", "patent_year")
Inventor <- c("inventor_city", "inventor_country", "inventor_county",
"inventor_county_fips", "inventor_first_name", "inventor_first_seen_date", "inventor_id",
"inventor_last_name", "inventor_last_seen_date", "inventor_lastknown_city",
"inventor_lastknown_country", "inventor_lastknown_latitude",
"inventor_lastknown_location_id", "inventor_lastknown_longitude",
"inventor_lastknown_state", "inventor_latitude", "inventor_location_id",
"inventor_longitude", "inventor_sequence", "inventor_state", "inventor_state_fips",
"inventor_total_num_patents")
Assignee <- c("assignee_city", "assignee_country", "assignee_county",
"assignee_county_fips", "assignee_first_name", "assignee_first_seen_date", "assignee_id",
"assignee_last_name", "assignee_last_seen_date", "assignee_lastknown_city",
"assignee_lastknown_country", "assignee_lastknown_latitude",
"assignee_lastknown_location_id", "assignee_lastknown_longitude",
"assignee_lastknown_state", "assignee_latitude", "assignee_location_id",
"assignee_longitude", "assignee_organization", "assignee_sequence", "assignee_state",
"assignee_state_fips", "assignee_total_num_inventors", "assignee_total_num_patents",
"assignee_type")
Gov <- c("govint_contract_award_number", "govint_org_id", "govint_org_level_one",
"govint_org_level_three", "govint_org_level_two", "govint_org_name",
"govint_raw_statement")
Citations <- c("appcit_app_number", "appcit_category", "appcit_date", "appcit_sequence",
"cited_patent_category", "cited_patent_date", "cited_patent_kind", "cited_patent_number",
"cited_patent_sequence", "cited_patent_title", "citedby_patent_category",
"citedby_patent_date", "citedby_patent_kind", "citedby_patent_number",
"citedby_patent_title")
CPC <- c("cpc_category", "cpc_first_seen_date", "cpc_group_id", "cpc_group_title",
"cpc_last_seen_date", "cpc_section_id", "cpc_sequence", "cpc_subgroup_id",
"cpc_subgroup_title", "cpc_subsection_id", "cpc_subsection_title",
"cpc_total_num_assignees", "cpc_total_num_inventors", "cpc_total_num_patents")
USPC <- c("uspc_first_seen_date", "uspc_last_seen_date", "uspc_mainclass_id",
"uspc_mainclass_title", "uspc_sequence", "uspc_subclass_id", "uspc_subclass_title",
"uspc_total_num_assignees", "uspc_total_num_inventors", "uspc_total_num_patents")
NBER <- c("nber_category_title", "nber_first_seen_date", "nber_last_seen_date",
"nber_subcategory_id", "nber_subcategory_title", "nber_total_num_assignees",
"nber_total_num_inventors", "nber_total_num_patents")

```

```

Lawyer <- c("lawyer_first_name", "lawyer_first_seen_date", "lawyer_id",
"lawyer_last_name", "lawyer_last_seen_date", "lawyer_organization", "lawyer_sequence",
"lawyer_total_num_assignees", "lawyer_total_num_inventors", "lawyer_total_num_patents")
Examiner <- c("examiner_first_name", "examiner_group", "examiner_id",
"examiner_last_name", "examiner_role")
Foreign <- c("forprior_country", "forprior_date", "forprior_docnumber", "forprior_kind",
"forprior_sequence")

```

```

f <- c(App, Pat, Inventor, Assignee, Gov, Citations)
Scraped_Data = as.data.frame(NULL)
for (i in 1:110){
  data<-search_pv(qry_funs$eq(patent_id=PatentList_Reissued[i]),fields = f)
  if (!is.null(data$data$patents)){
    v <- as.data.frame(data$data$patents)
    v0 <- v[,1:29]
    v0a <- t(apply(v0, 2, paste, collapse="; "))
    v1 <- as.data.frame(data$data$patents$assignees)
    v1a <- t(apply(v1, 2, paste, collapse="; "))
    v2 <- as.data.frame(data$data$patents$inventors)
    v2a <-t(apply(v2, 2, paste, collapse="; "))
    v3 <- as.data.frame(data$data$patents$applications)
    v3a <- t(apply(v3, 2, paste, collapse="; "))
    v4 <- as.data.frame(data$data$patents$application_citations)
    v4a <- t(apply(v4, 2, paste, collapse="; "))
    v5 <- as.data.frame(data$data$patents$cited_patents)
    v5a <- t(apply(v5,2,paste,collapse="; "))
    v6 <- as.data.frame(data$data$patents$citedby_patents)
    v6a <- t(apply(v6,2,paste,collapse="; "))
    v7 <- as.data.frame(data$data$patents$gov_interests)
    v7a <- t(apply(v7, 2, paste, collapse="; "))
    v_comb <- cbind(PatentList_Reissued[i],v0a,v1a,v2a,v3a,v4a,v5a,v6a,v7a)
    Scraped_Data <- rbind(Scraped_Data,v_comb)
  }
  else {
    v_comb <- as.data.frame(cbind(PatentList_Reissued[i],t(rep(NA,105))))
    names(v_comb)<-names(Scraped_Data)
    Scraped_Data <- rbind(Scraped_Data,v_comb)
  }
  print(i)
}

```

```

Folder = "C:/Users/rkn3/Dropbox (Partners HealthCare)/DOPE/5. Patent Data"
setwd(Folder)
write.csv(Scraped_Data,file = "Scraped Data Reissued 1-110.csv")

```

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