Trends in US New Drug Approvals

2015 FDA New Drug Approvals (Compared to Approvals in Previous Years)

Key Findings

- A record number of 45 new drugs (including 12 new biologics) was approved by FDA in 2015 (up from 41 approvals in 2014 and 27 in 2013). 2015 also shows record approval numbers for new biologics (12), new cancer drugs (15), new orphan drugs (21) and potential "blockbusters" (17).
- Worldwide peak sales potential from new drugs approved in 2015 was estimated to be $57 billion (as compared to $43 billion peak sales estimates for drugs approved in 2014 and $36 billion for drugs approved in 2013). Average worldwide peak sales potential for new drugs approved in 2015 reached $1.4 billion.
- Novartis received 4 new drug approvals in 2015, followed by Allergan (3). The new Novartis drugs approved have a combined peak sales potential of over $8 billion. Over the past 4 years (2012-2015), Roche and Johnson & Johnson share the number 1 spot, with 7 approvals each. However, Gilead with 5 approvals can expect the highest peak sales out of all companies obtaining new drug approvals in this period.
- 15 new cancer drugs were approved in 2015 (compared to an average of 9-10 such approvals in previous years) with a total peak sales potential of $17.7 billion. 2015 was also a very strong year for cardiovascular drugs (6 approvals, peak sales estimates $10.8 billion). Higher than usual approval numbers were also observed in some other therapeutic areas such as metabolic/endocrinology, genetic diseases and CNS/pain.
- In 2015, the 21 new orphan drugs approved accounted for close to 50% of all approvals.
- The majority of new drug approvals in each year since 2008 originated at smaller biopharma, i.e. companies outside of the 30 largest biopharma companies. 23 (or 51%) of all new drugs approved in 2015, were in-licensed or acquired through M&A with large pharma active mostly on the "buy side" and smaller companies active on the "sell side" and – to a lesser degree – on the "buy side".

Additional key data of new drugs approved by the FDA since 2003 is available under www.hbmpartners.com/report. The use of data and charts is permitted with reference to "HBM Partners – Trends in New Drug Approvals".

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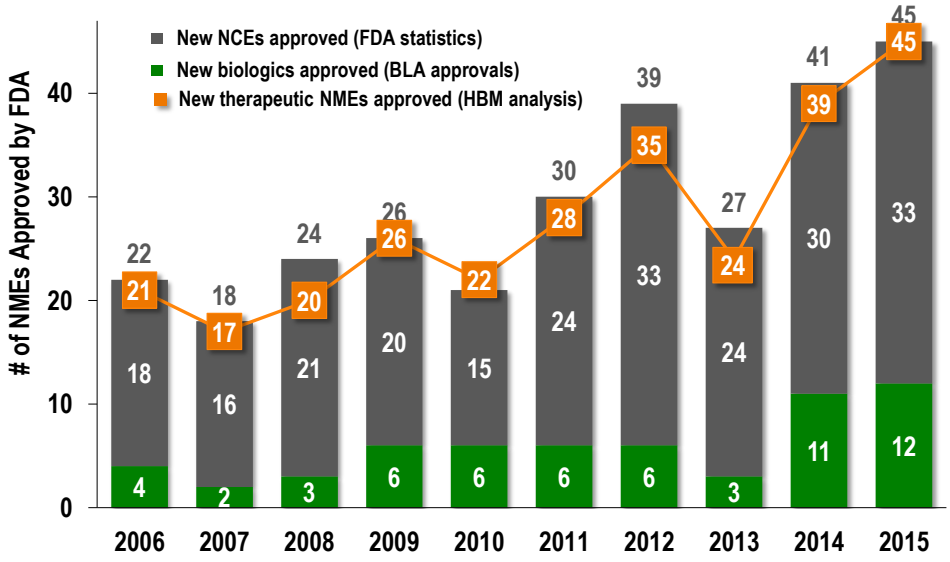
New Drug Approvals by FDA in 2015

Comment: The term "new drug" in this report is used for new therapeutic molecular entities ("NMEs"). This includes new chemical entities ("NCEs") and new biologics (classified by FDA as NMEs). It does not include (a) new non-therapeutic agents such as imaging agents, preventive vaccines etc., some which have been included in the FDA approval numbers and reports), (b) BLA approvals (by CBER) such as fractioned plasma products etc. (which are not classified as NMEs), (c) approvals of existing drugs for new indications, and (d) new combinations of previously approved NMEs.

New Drug (NME) Approvals by FDA



Source: FDA (www.fda.gov), HBM Analysis

A record number of 45 new drugs (new therapeutic molecular entities or "NMEs") was approved by FDA in 2015. Since a low in 2007, the number of new NMEs approved in the US has shown a clear upward trend. In 2013, John Jenkins, Director of the FDA's Office of New Drugs, mentioned in a presentation that the high approval number in 2012 were "not the new normal" [expecting lower numbers, more in-line with long-term averages such as in 2013]. The high approval numbers in 2014 and 2015 hopefully indicate that the "new normal" number of drug approvals going forward might be in the forties or at least in the thirties per year.

As we highlight later in this report, potential peak sales of newly approved drugs (in each year) have also steadily increased (even in 2013 despite fewer approvals).

2015 also saw record approval numbers for new biologics (12 vs 11 in 2014, 3 in 2013), new cancer drugs (15 vs 9 in 2014, 8 in 2013), new orphan drugs (21 vs 17 in 2014, 9 in 2013) and potential "blockbusters" (17 vs 15 in 2014, 14 in 2013).

Further Reading

In recent years, the FDA has published a comprehensive annual report on new drugs approvals. The 2015 report can be found under this link:
http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM485053.pdf

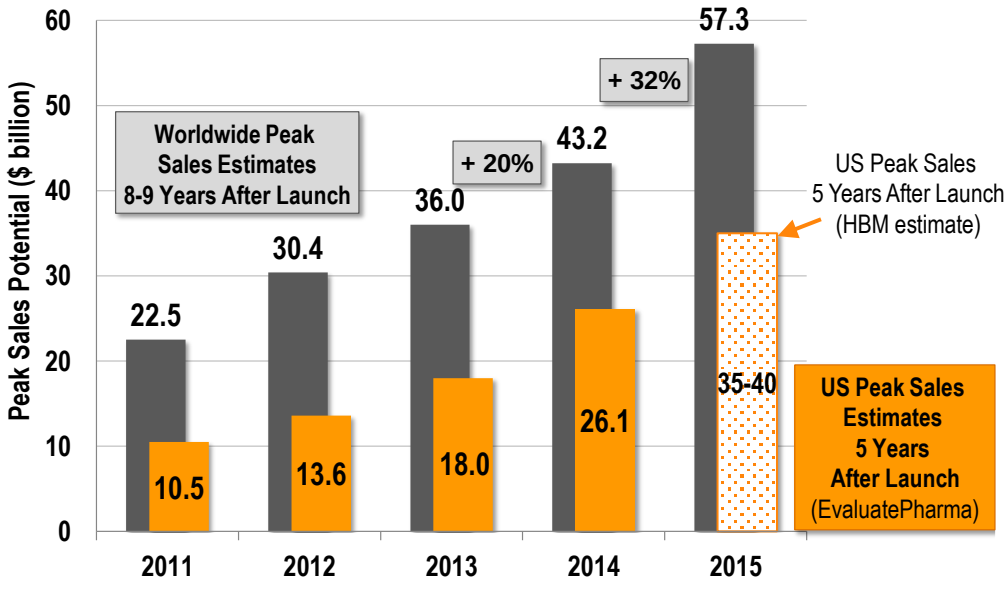
Please note that in earlier such FDA reports (before 2013) a cut-off date before year-end had been used, and thus these reports do not include all new drugs approved in the respective year.

A good overview of 2015 new drug approvals is also available by FierceBiotech:
http://www.fiercebiotech.com/story/biggest-winners-and-losers-2015-race-new-drug-approvals/2016-01-04

Peak Sales Potential of New Drugs Approved in 2011-2015

Comment: Estimated annual peak sales of NMEs approved were collected from analyst reports and other sources. In case of several or differing estimates we calculated the averages. Please note that in our analysis, we use the worldwide peak sales of the new drugs as estimated at the time of approval. Thus, we do not adjust the figures retrospectively when actual sales figures or new estimates are available. Peak sales estimates cited by other sources sometimes take expected sales 5 years after approval (while peak sales usually are reached in years 8-9 post-approval) and for the US market only. Such US sales estimates 5 year after launch (orange bars in chart below, source EvaluatePharma) are about 40% to 50% lower than our worldwide peak sales estimates.

Estimated Peak Sales Potential of New Drugs (NMEs) Approved by FDA



Source: FDA (www.fda.gov), HBM analysis

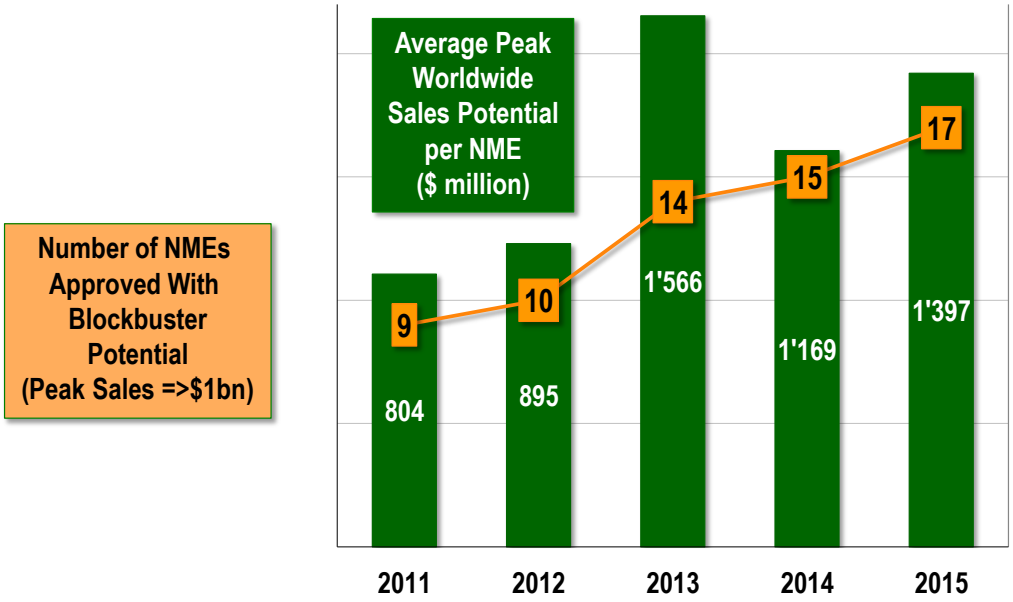
The overall expected worldwide peak sales of newly FDA-approved drugs in 2015 is close to $60 billion and 32% higher than the respective number for 2014. Forecasts for US-only sales 5 years after approval (from EvaluatePharma) are significantly lower and we estimate such US sales estimates for drugs approved in 2015 to be around $35-40 billion.

Worldwide peak sales potential of newly FDA-approved biologics (mainly antibodies) also rose strongly to approximately $16 billion for both 2014 and 2015 (see below):

	2011	2012	2013	2014	2015
# of biologics approved	6	6	3	11	12
Peak Sales Estimates ($bn) of Biologics Approved	**6.1**	**3.6**	**4.8**	**16.1**	**15.8**

Number of Potential Blockbusters

Number of New Potential Blockbusters and Average Estimated Peak Sales for New Drugs Approved



Source: FDA (www.fda.gov), HBM Analysis

In 2015, 17 newly approved drugs or 38% of the total have "blockbuster" potential, i.e. worldwide sales could reach over $1 billion per year. The number of approved potential blockbusters has almost doubled since 2011.

Among the 17 potential blockbusters approved in 2015, 5 were new cancer drugs (vs 4 in 2014), 3 were new cardiovascular drugs (vs 0 in 2014), 2 were new anti-virals (vs 2 in 2014) and 2 were new drugs approved in diabetes/metabolic/endocrinology as well as in immunology. The list of potential blockbusters approved since 2013 can be found on the next page.

The average peak sales potential per newly approved drug is trending upwards and has reached $1.4 billion in 2015.

List of New "Blockbuster" Drugs Approved 2013-2015

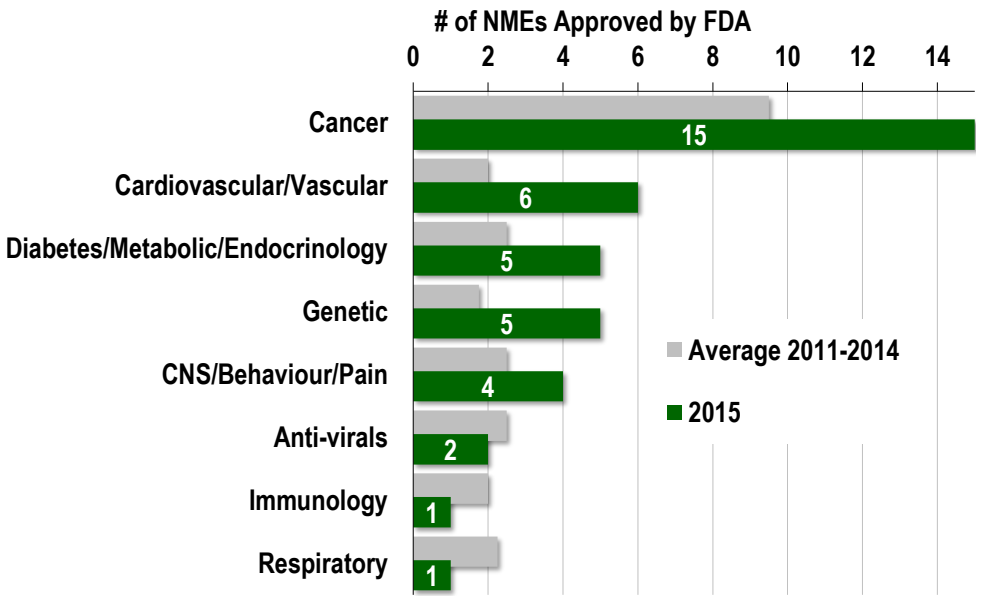
(With a worldwide peak sales estimate at time of approval of $1 billion or more)

Year	Drug Name (Ingredient) / Drug Sponsor / Indication	Worldwide Peak Sales Estimate ($bn)
2013	Sovaldi (sofosbuvir) / Gilead Sciences (USA) / Hepatitis C	5.7
	Imbruvica (ibrutinib) / Johnson & Johnson (USA) / Blood cancer	5.3
	Kadcyla (ado-trastuzumab emtasine) / Roche (Switzerland) / Breast cancer	3.0
	Anoro Ellipta (umeclidinum and vilanterol) / GlaxoSmithKline (UK) / COPD	2.9
	Tecfidera (dimethyl fumarate) / Biogen Idec (USA) / Multiple Sclerosis	2.8
	Breo Ellipta (fluticasone furoate; vilanterol trifenatate) / GlaxoSmithKline (UK) / COPD	2.0
	Brintellix (vortioxetine) / Takeda (Japan) / Depression	1.8
	Gazyva (obinutuzumab) / Roche (Switzerland) / Blood cancer	1.8
	Invokana (canagliflozin) / Johnson & Johnson (USA) / Diabetes type 2	1.5
	Gilotrif (afatinib) / Boehringer Ingelheim (Germany) / Lung cancer	1.3
	Pomalyst (pomalidomide) / Celgene (USA) / Blood cancer	1.2
	Tivicay (dolutegravir) / ViiV Healthcare (UK) / HIV-1	1.2
	Opsumit (macitentan) / Actelion (Switzerland) / Pulmonary arterial hypertension	1.0
	Xofigo (radium RA 223 dichloride) / Bayer (Germany) / Prostate cancer	1.0
2014	Harvoni (ledipasvir/sofosbuvir) / Gilead Sciences (USA) / Hepatitis C	10.0
	Opdivo (nivolumab) / Bristol-Myers Squibb (USA) / Skin cancer	4.5
	Keytruda (pembrolizumab) / Merck & Co. (USA) / Skin cancer	2.7
	Viekira Pak (ombitasvir, paritaprevir, ritonavir, dasabuvir) / AbbVie (USA) / Hepatitis C	2.3
	Plegridy (peginterferon beta-1a) / Biogen Idec (USA) / Multiple Sclerosis	1.8
	Otezla (apremilast) / Celgene (USA) / Psoriasis	1.8
	Sylvant (siltuximab) / Johnson & Johnson (USA) / Rare lymphatic system disease	1.5
	Cyramza (ramucirumab) / Eli Lilly (USA) / Stomach cancer	1.4
	Ofev (nintedanib) / Boehringer Ingelheim (Germany) / Idiopathic pulmonary fibrosis (IPF)	1.4
	Esbriet (pirfenidone) / Roche (Switzerland) / Idiopathic pulmonary fibrosis (IPF)	1.4
	Zydelig (idelalisib) / Gilead Sciences (USA) / Blood cancer	1.3
	Trulicity (dulaglutide) / Eli Lilly (USA) / Diabetes type 2	1.3
	Farxiga (dapaglifozin) / AstraZeneca (UK) / Diabetes type 2	1.2
	Entyvio (vedolizumab) / Takeda (Japan) / Autoimmune disease	1.2
	Zerbaxa (ceftolozane/tazobactam) / Merck & Co. (USA) / Bacterial infections	1.1
2015	Orkambi (lumacaftor 200 mg/ ivacaftor 125 mg) / Vertex Pharmaceuticals (USA) / Cystic fibrosis	5.2
	Entresto (sacubitril/valsartan) / Novartis (Switzerland) / Chronic heart failure	5.1
	Ibrance (palbociclib) / Onyx Pharmaceuticals (USA) / Breast cancer	4.4
	Praluent (alirocumab) / Regeneron Pharmaceuticals (USA) / Hypercholesterolemia (HeFH), artheroscle	3.5
	Repatha (evolocumab) / Amgen (USA) / Hypercholesterolemia (HeFH), artherosclerosis	3.2
	Tresiba (insulin degludec injection) / Novo Nordisk (Denmark) / Diabetes type 1 and 2	3.1
	Genvoya (elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide) / Gilead Sciences (USA) / HIV-1	3.0
	Darzalex (daratumumab) / Genmab (Denmark) / Multiple myeloma	2.5
	Tagrisso (osimertinib) / AstraZeneca (UK) / Lung cancer	2.4
	Alecensa (alectinib) / Chugai Pharmaceutical (Japan) / Lung cancer	2.2
	Rexulti (brexpiprazole) / Otsuka Pharmaceutical (Japan) / Schizophrenia, depression	2.2
	Cosentyx (secukinumab) / Novartis (Switzerland) / Psoriasis	2.0
	Ninlaro (ixazomib) / Millenium Pharmaceuticals (USA) / Multiple melanoma	1.7
	Uptravi (selexipag) / Nippon Shinyaku (Japan) / Pulmonary arterial hypertension	1.5
	Nucala (mepolizumab) / GlaxoSmithKline (UK) / Asthma	1.3
	Kanuma (sebelipase alfa) / Synageva (USA) / Enyzme replacement (Wolman's Disease)	1.0
	Daklinza (daclatasvir) / Bristol-Myers Squibb (USA) / Hepatitis C	1.0
	Empliciti (elotuzumab) / PDL Biopharma (USA) / Multiple melanoma	1.0
	Veltassa (patiromer for oral suspension) / Relypsa (USA) / Hyperkalemia	1.0

Note: Drug sponsor = drug owner at time of approval

New Drug Approvals by Therapeutic Area

Number of New Drugs (NMEs) Approved by Indication

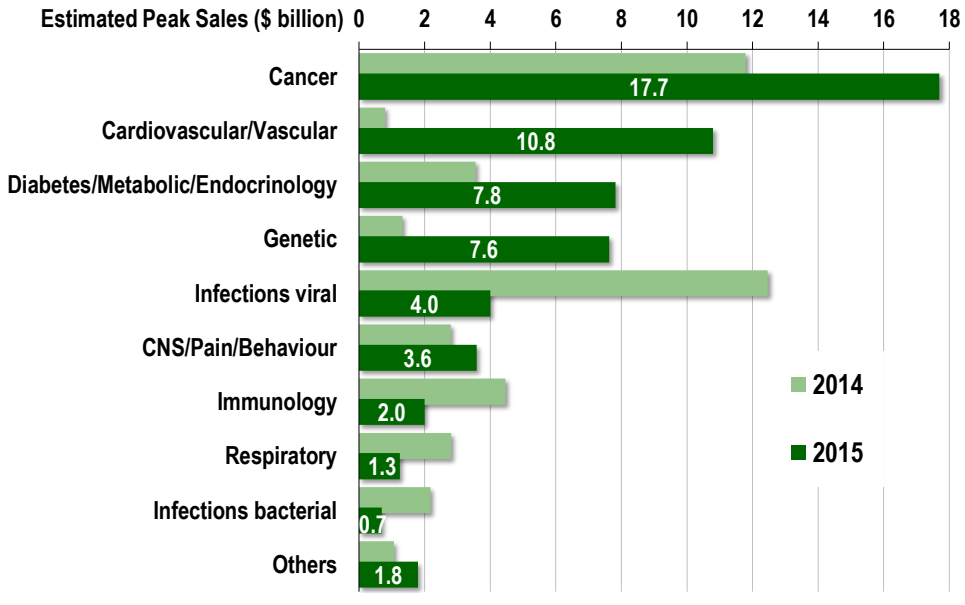


Source: FDA (www.fda.gov), HBM Analysis

15 new cancer drugs were approved in 2015 (compared to an average of 9-10 approvals for previous years). Drugs in cardiovascular, diabetes/metabolic/endocrinology, genetic diseases and CNS also showed a significant increase of approvals.

New cancer drugs approved in 2015 are estimated to generate close to $18 billion peak sales (31% of total peak saled of drugs approved in 2015). In 2014, the respective percentage was 27%. The "megabuster" Harvoni approved in 2014 led to high potential peak sales of new anti-virals approved in that year. Peak sales of anti-virals approved in 2015 were down to more "normal" levels. New drugs for cardiovascular, metabolic and genetic diseases are also expected to generate high sales.

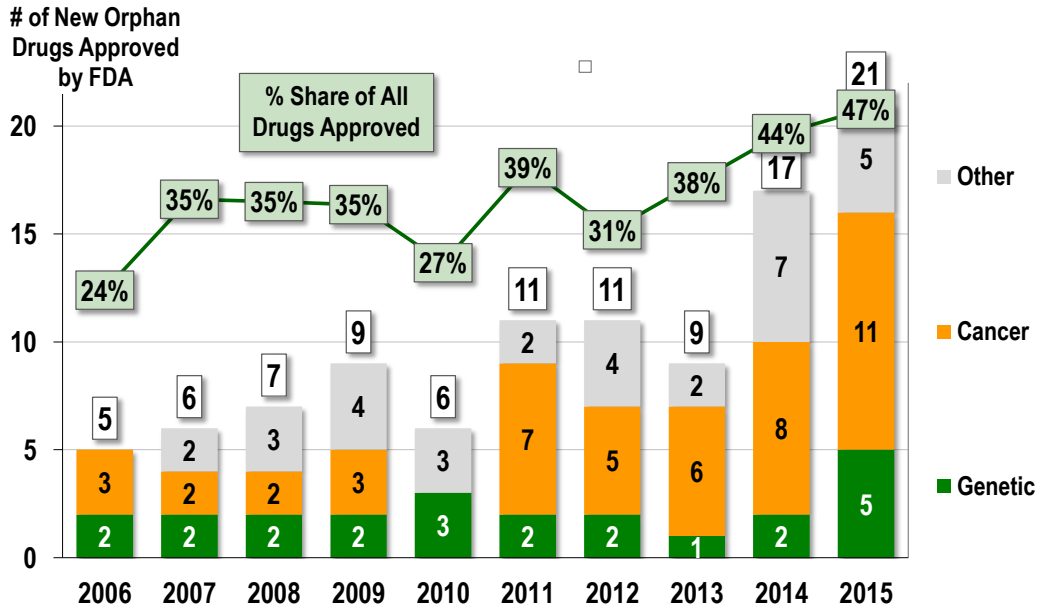
Peak Sales Potential of New Drugs (NMEs) Approved by Therapeutic Area



Source: FDA (www.fda.gov), HBM analysis

New Orphan Drugs Approved

New Orphan Drugs Approved by FDA

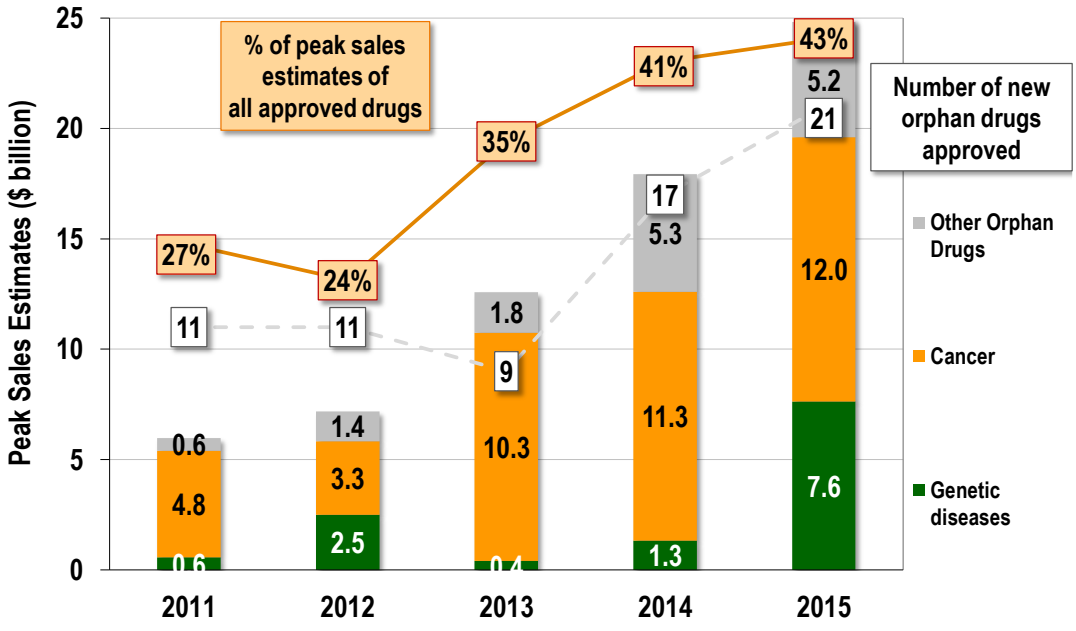


Source: FDA (www.fda.gov), HBM analysis

In 2015, a record number of 21 orphan drugs was approved, accounting for almost 50% of all approvals.

The chart below shows that the total peak sales potential of orphan drugs approved in 2015 has surpassed $20 billion, with major drugs approved in rare genetic diseases and orphan malignancies mainly. 2015 numbers include Orkambi, a new cystic fibrosis drug with sales potential of $5 billion. The average peak sales potential of newly approved orphan drugs has exceeded $1 billion since 2013 (and thus is not much lower than for other new drugs).

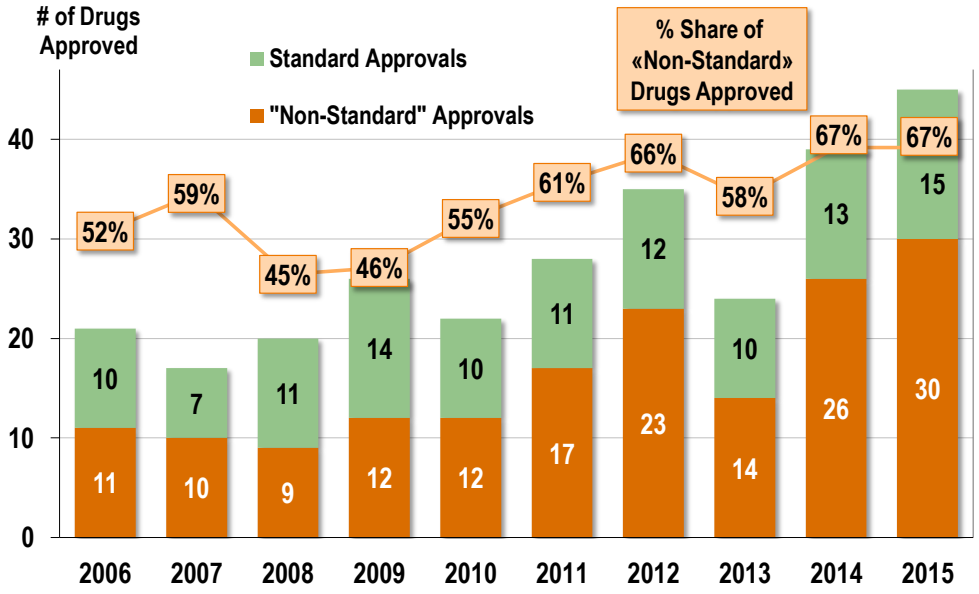
Peak Sales Potential of New Orphan Drugs Approved



Source: FDA (www.fda.gov), HBM analysis

Priority Reviews, Accelerated Approvals, Breakthrough Therapies etc.

Standard and "Special" (Non-Standard) New Drug Approvals by FDA



Source: FDA (www.fda.gov), HBM analysis

There are several regulatory paths provided by the FDA to expedite the drug development and approval process. These various initiatives are targeted mainly at diseases for which no effective therapies exist or where there is a high unmet medical need. The initiatives "Fast Track", "Priority Review" and "Accelerated Approvals" have been in place for quite a while. In 2015, 22 (!) new NMEs were approved under the "Breakthrough Therapy" designation introduced only in 2012. Furthermore, Avycaz and Cresemba were approved under the new "Qualified Infectious Disease Program" (QIDP).

The chart above shows the number of approvals under any of the above-mentioned accelerated regulatory paths (including "Orphan Drug" designation). The number of these "non-standard"" approvals has picked up starting from a low in 2008, and – during the last two years – two thirds of new drugs fell into this category. The number of drugs approved under "special" designations in 2015 were (in declining order): Priority Review (24), Breakthrough Therapies (22), Orphan (21), Fast Track (14), Accelerated Approvals (6) and QIDP (2).

"First-In Class" Drugs Approved

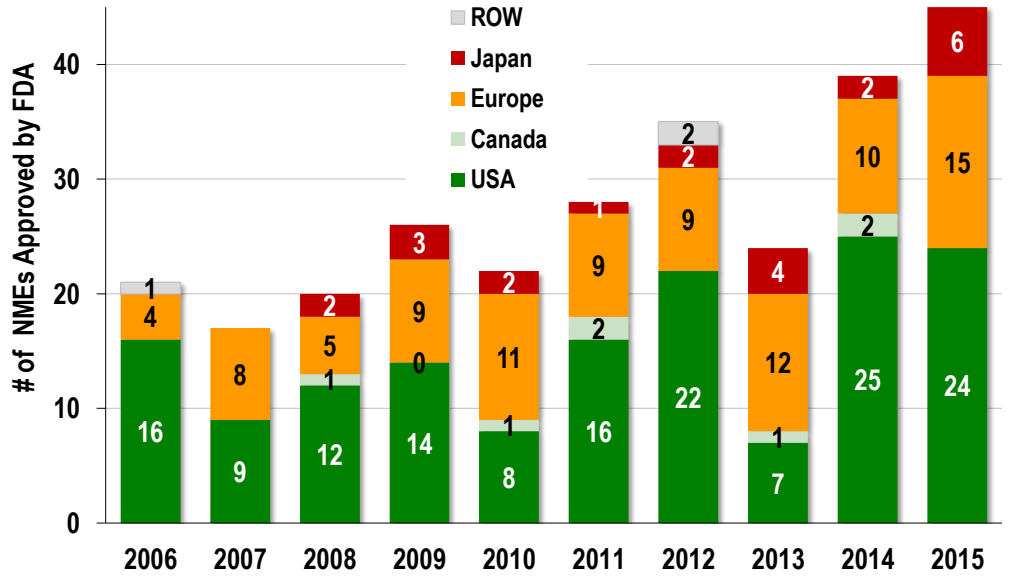
16 (or 36%) of the 45 new drugs approved in 2015 were classified by FDA as "first-in-class", i.e. with a new mechanism different from existing drugs. The number of such approvals has been quite high since 2011. Before that, only about 4-8 first in-class new drugs were approved each year. It seems that the broad scientific discovery efforts by industry and publicly-funded institutions started to bear fruit. It is encouraging to see that biopharma companies push forward the development of genuinely new drugs.

	2011	2012	2013	2014	2015
# of new drug approved	28	35	24	39	45
# of new "first-in-class" drug approved	**13**	**19**	**9**	**16**	**16**
% of all drugs approved	46%	54%	38%	41%	36%

New Drugs Approved by Location of Drug Sponsor/Owner

Comment: The "Drug Sponsor/Owner" is the company that owns the drug at time of approval or has licensed it for the US or worldwide markets. "Location" is the location of the company's headquarter.

New Drug Approvals (NMEs) by Location/Headquarter of Drug Sponsor/Owner



Source: FDA (www.fda.gov), HBM analysis

US (and European) companies continue to dominate the US drug approval ranks. Japanese pharma companies also had a good year with 6 approvals in 2015. Companies located in the "rest of the world" still play an insignificant role as sponsors of new drugs approved in the US.

Companies with Highest Potential Peak Sales from New Drugs (NMEs)

The table below lists the companies with the highest potential sales from new drugs approved in 2015 and in the 2012-2015 period. The drugs are assigned to the company that owned the drug at the time of approval or had US/worldwide marketing rights.

In 2015, Novartis came out on top with 4 (!) approvals and corresponding total peak sales of over $8 billion. Allergan/Actavis had 3 approvals.

The top 15 positions, for both 2015 and 2012-2015, are dominated by the incumbent large pharma companies with the exception of Vertex which, thanks to the approval of cystic fibrosis drug Orkambi, ranked second for peak sales of drugs approved in 2015. For the 2012-2015 period, Gilead can expect the highest peak sales from its 5 approvals.

Peak Sales Estimates of New Drugs Approved by Company

New Drugs Approved in 2015

Rank	Company	# of Drugs Approved 2015	Peak Sales Estimates ($bn)
1	Novartis	4	8.1
2	Vertex Pharmaceuticals	1	5.2
3	Pfizer	1	4.4
4	Sanofi	1	3.5
5	Amgen	2	3.5
6	AstraZeneca	2	3.1
7	Novo Nordisk	1	3.1
8	Gilead Sciences	1	3.0
9	Roche	2	2.8
10	Otsuka Pharmaceutical	2	2.5
11	Johnson & Johnson	2	2.5
12	Bristol-Myers Squibb	2	2.0
13	Alexion	2	1.8
14	Takeda	1	1.7
15	Allergan/Actavis	3	1.6
16	Actelion	1	1.5
17	GlaxoSmithKline	1	1.3
18	Relypsa	1	1.0
19	Alkermes	1	0.8
20	Shire	1	0.6

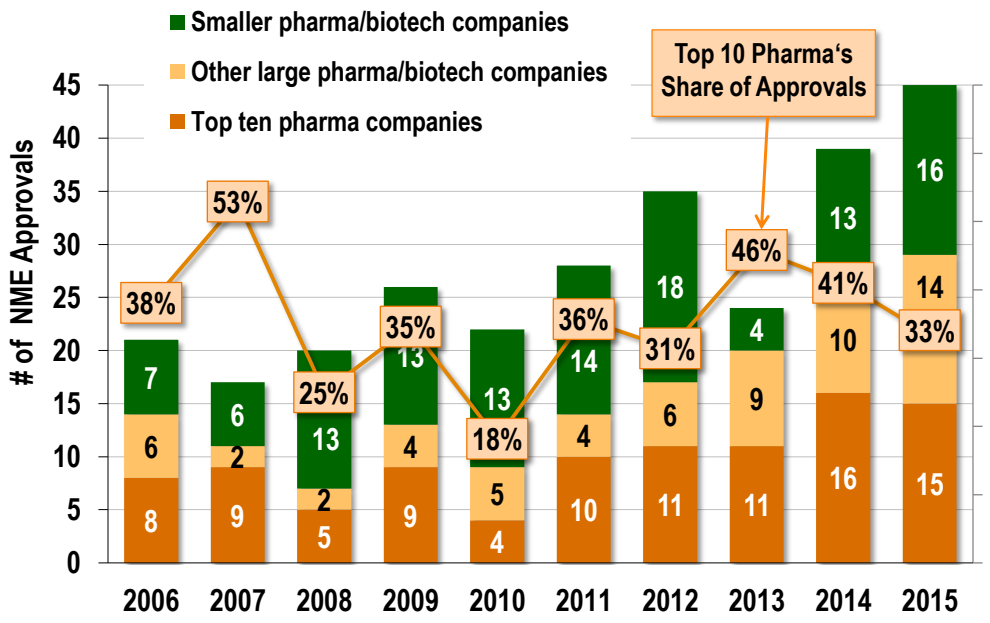
New Drugs Approved 2012-2015

Rank	Company	# of Drugs Approved 2012-2015	Peak Sales Estimates ($bn)
1	Gilead Sciences	5	21.7
2	Roche	7	12.3
3	Johnson & Johnson	7	11.3
4	Bristol-Myers Squibb	5	10.5
5	Novartis	6	8.8
6	Pfizer	6	8.3
7	GlaxoSmithKline	6	7.3
8	Vertex Pharmaceuticals	2	7.3
9	Sanofi	5	5.5
10	Takeda	4	5.5
11	Merck & Co.	6	5.1
12	AstraZeneca	5	5.1
13	Biogen Idec	2	4.6
14	Amgen	3	3.8
15	Eli Lilly	4	3.7
16	Novo Nordisk	1	3.1
17	Celgene	2	3.0
18	Boehringer Ingelheim	4	2.8
19	Actelion	2	2.5
20	Otsuka Pharmaceutical	2	2.5

New Drug Approvals by Large Pharma

Definitions: "Top ten pharma companies" = Pharma companies ranked within the top ten worldwide by pharma sales. "Other large pharma/biotech companies" =Biopharma companies ranked between 11 and 30 in terms of worldwide sales (Note: Gilead is included in this group even though Gilead moved into the top ten in 2014), "Smaller pharma/biotech companies" = Other (smaller) biopharma companies.

New Drugs (NMEs) Approved by Size of Drug Sponsor/Owner



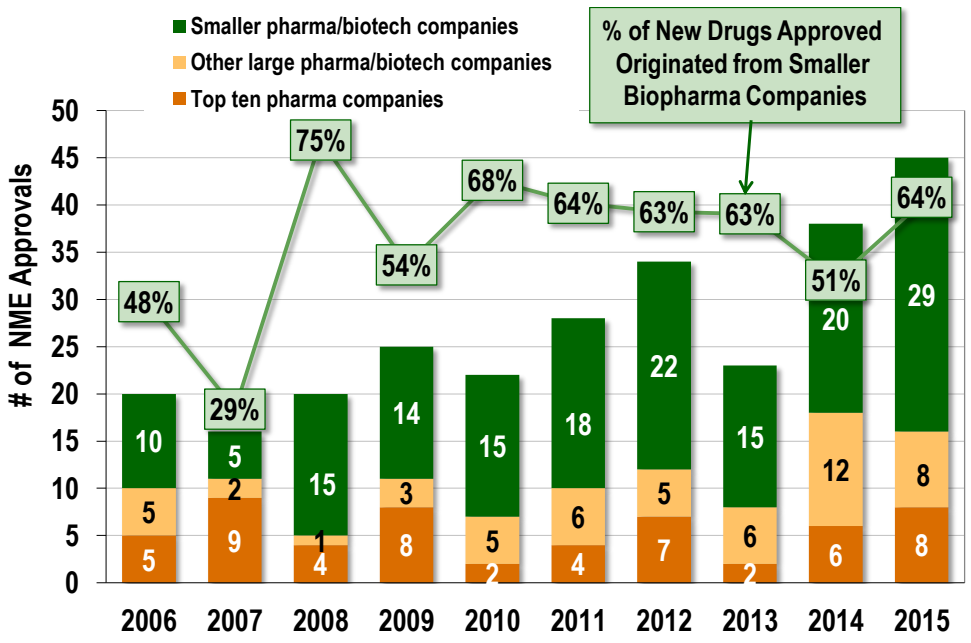
Source: FDA (www.fda.gov), HBM analysis

The chart above shows that the 33% share of approvals, accounted for by the top ten pharma companies in 2015, approximate the long-term average. It may seem that R&D at large pharma has become more productive again with a jump in approvals in 2011 and thereafter. However, not all such approved drugs were developed in-house. In fact, out of 15 new approvals by "top ten" pharma in 2015, only 6 were discovered in-house (while 6 were in-licensed and 3 were acquired through company acquisitions before approval). For the ten years from 2006 to 2015, drugs developed in-house by the "top ten" pharma companies account for less than 20% of all approved drugs.

Originators of New Drugs Approved

Comment: The "Drug Originator" is defined here as the company that undertook the first significant development effort for a drug. Many drugs were fully discovered and developed within a biopharma company. Some other new compounds were originally discovered by universities or other research institutions, and then transferred to a biopharma company (also referred to as "Drug Originator" herein) for further development.

New Drugs (NMEs) Approved by Size of Drug Originator

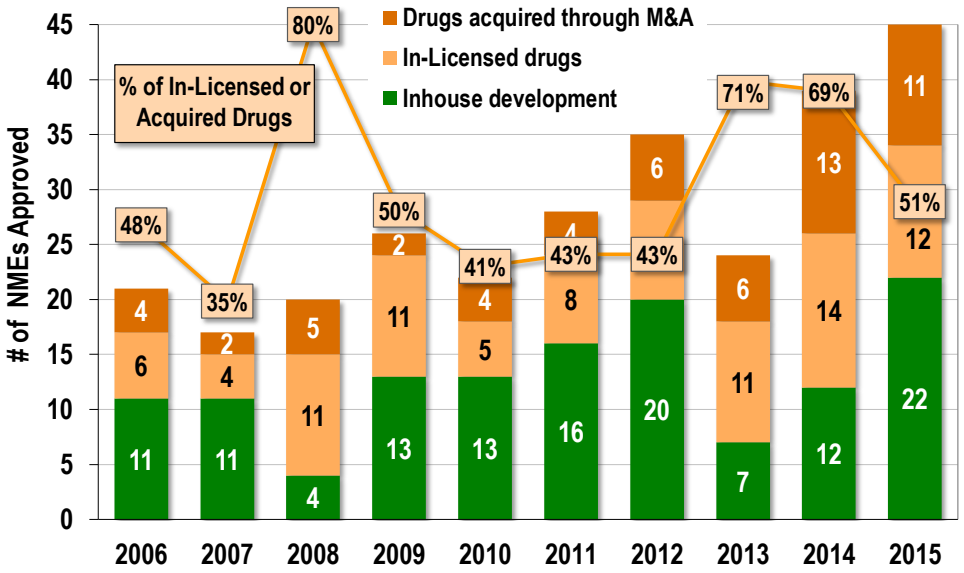


Source: FDA (www.fda.gov), HBM analysis

The majority of new drug approved by FDA in 2015 (and the years before) originated at smaller companies (i.e. companies outside of the largest 30 biopharma companies). As these smaller companies often out-license their drug candidates or get acquired before approval, the number of approvals in their name (16 in 2015) understates their important contribution to the development of new drugs. As already noted, smaller companies are also active on the in-licensing and acquisition side.

Internal vs External Innovation

New Drugs (NMEs) Approved – In-House Development vs. In-Licensed or Acquired Through M&A



Source: FDA (www.fda.gov), HBM analysis / Note: Information not available for one NME in 2013.

About half of the drugs approved in 2015 were in-licensed or acquired through M&A. The high proportion of "externally" licensed or acquired drugs is not a new phenomenon. In addition, companies of all sizes are active both on the "buy" and "sell" side. With the recent surge in biopharma M&A activity, we expect that especially larger companies will derive more of their future drug approvals from externally sourced compounds.

In general, larger companies have a higher proportion of approved drugs that were in-licensed or acquired (vs. in-house developed drugs). In fact, only about 30% to 40% of approved drugs developed by the top ten pharma companies originated in-house, whereas in the case of smaller companies this number is usually over 50%.

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