

HBM New Drug Approval Report

Analysis of FDA New Drug Approvals in 2018 (and Multi-Year Trends)

Also available online with data of all new drugs approved by FDA since 2003

<http://www.hbmpartners.com/en/industry-reports>

Further Reading:

FDA 2018 New Drug Approval Report:

<https://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm592464.htm>

Fierce Biotech – List of new drugs approved in 2018:

<https://www.fiercebiotech.com/special-report/two-years-after-sluggish-2016-new-drug-approvals-hit-their-stride-2018>

For questions, comments or corrections please contact the authors of this report

Dr Ulrich Geilinger, ulrich.geilinger@hbmpartners.com and Dr Chandra Leo, chandra.leo@hbmpartners.com

January 2019

The use of data and charts is permitted with reference to “HBM New Drug Approval Report”

2018 New US Drug Approvals - Summary

- Record number of 59 (or 57*) new drugs (NMEs = New Molecular Entities) approved by FDA in 2018
- Peak sales potential of new drugs approved in 2018 lower than in some previous years
- Lower number of new potential blockbusters approved (13 in 2018 vs. 23 in 2017)
- Most new drugs approved in 2018 target orphan or niche indications, 33 (or 68%) of new drugs with Orphan Designation
- Record number of 11 new drugs approved target rare genetic diseases
- Close to 50% of all new drugs approved in 2018 are owned by smaller, innovative biopharma companies (outside of the largest 50 pharma companies).
- Accessing novel drug candidates by licensing and acquisition has become more important. And, on average, less than 50% of approvals stem from inhouse development efforts (true for company of all sizes).

* HBM counts only 57 NMEs vs. FDA's 59, see slide 3

FDA Drug Approval Numbers 2018 (and 2017)

59* NMEs
approved (46)

21 "First-in-
class" drugs (14)

\$40 billion
peak sales
potential
(\$50 billion)

13 potential
blockbusters (23)

33 "Orphan"
drugs (17)

11 rare
genetic
disease
drugs (5)

5 immunology
drugs (4)

16 cancer
drugs (13)

5 anti-virals (3)

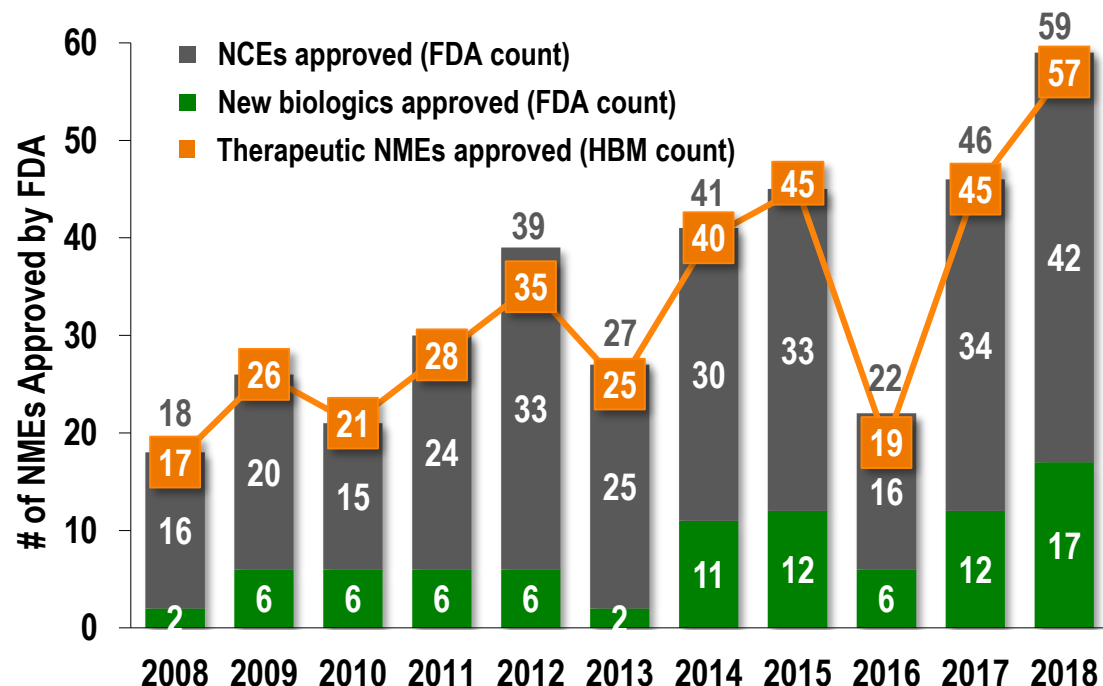
4 antibiotics (4)

4 CNS/pain
drugs (2)

7 Priority Review
Vouchers awarded (6)

Record Number of New Drugs Approved by FDA in 2018

New Drugs (NMEs) Approved by FDA 2008-2019 (CDER Approvals)



Source: FDA, HBM analysis

NME = new molecular entity, NCE = new chemical entity, i.e. small molecule

- Highest number of new drug approvals ever (topping the 53 approvals in 1996)
- Record number NCEs (42) and biologics (17) approved
- However, lower average peak sales expected from new drugs approved in 2018

FDA's CDER approved 59 NMEs (New Molecular Entities) in 2018.

In the HBM analysis, we counted only with 57 NMEs:

Braftovi/Mektovi, a combination drug, is only counted as one NME in our analysis

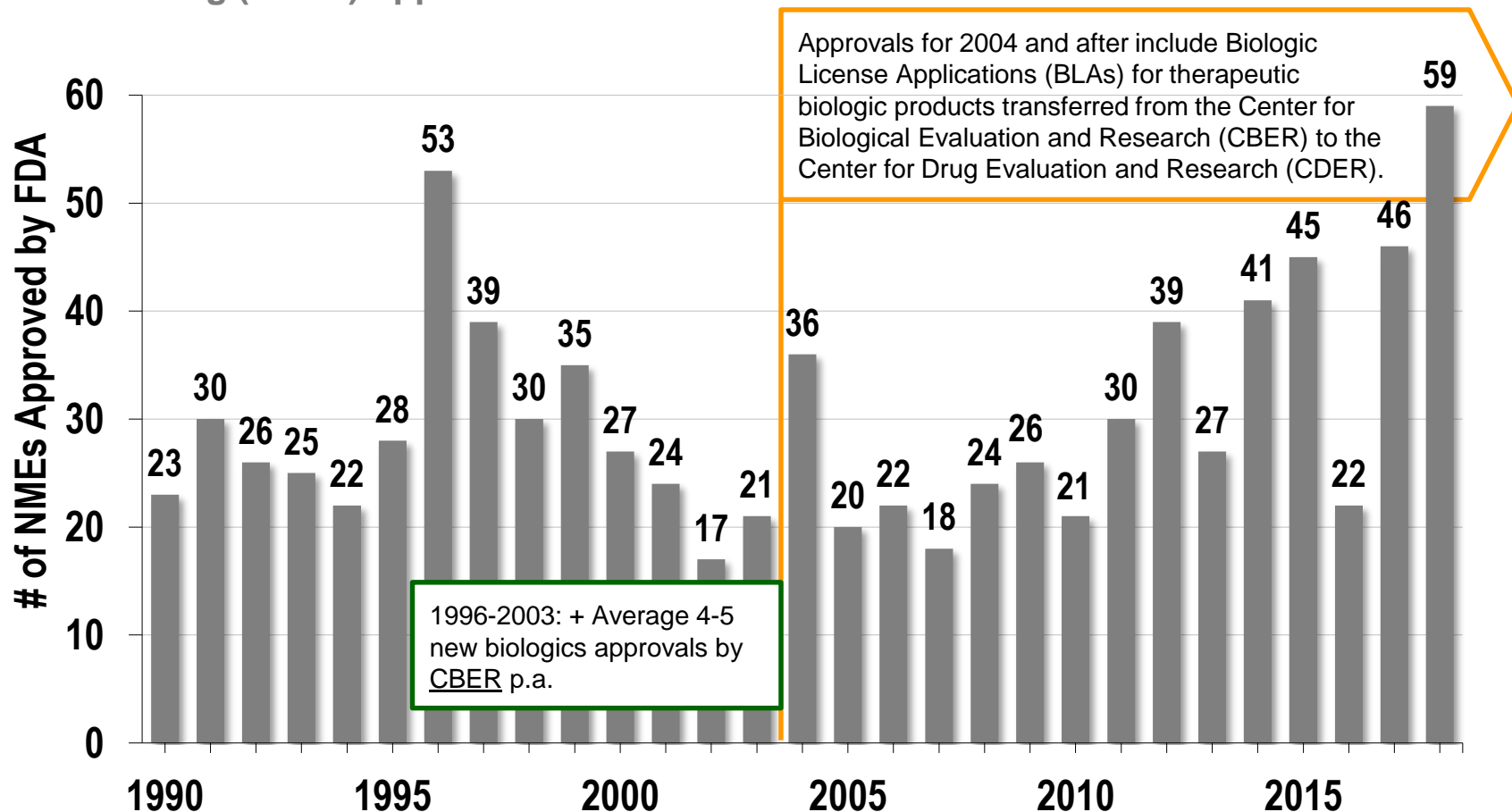
Injectable **Akynzeo** was omitted as the combination drug was already approved as an oral version in 2014.

There were also new biologics approved by **CBER** in 2018 that could be considered NMEs such as **Jivi** (Hemophilia A bleeding control) and **Andexxa** (anitcoagulant reversal). These are not included in the HBM analysis.

In previous years, new drugs counted by FDA as NMEs also included certain diagnostic or other non-therapeutic agents. Thus, our count of NMEs in some years is slightly lower than the official FDA NME count.

FDA New Drug Approvals – Looking Back to 1990

New Drug (NMEs) Approvals 1990-2018



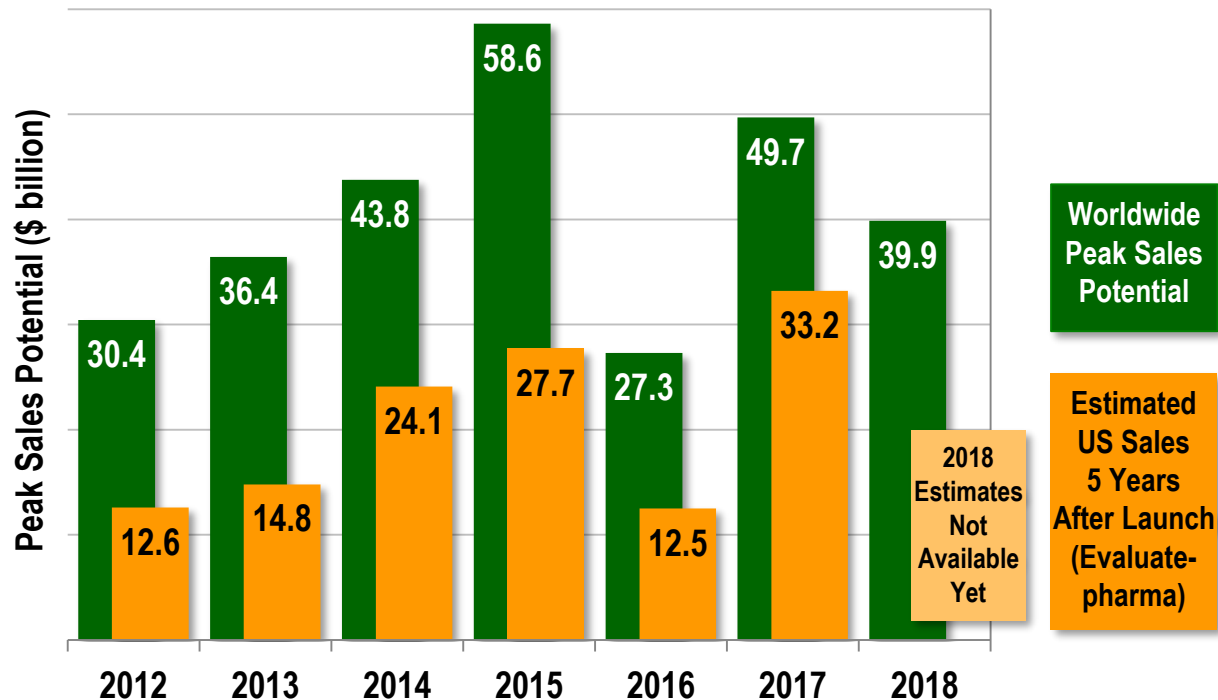
Source: FDA, "Summary of NDA Approvals & Receipts, 1938 to the present"

<https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm2006085.htm>

Market Potential of 2018 Approvals Below Previous Highs

Worldwide Peak Sales Potential of New Drugs Approved 2012-2018

(including expected US sales 5 years after approval)



Source: EvaluatePharma, HBM Analysis (from various sources)

Despite a record number of FDA approvals in 2018, estimated peak sales for all drugs* approved in 2018 is lower than in some previous years.

Most new drugs approved in 2018 target niche or orphan markets and few (13) have “blockbuster” potential.

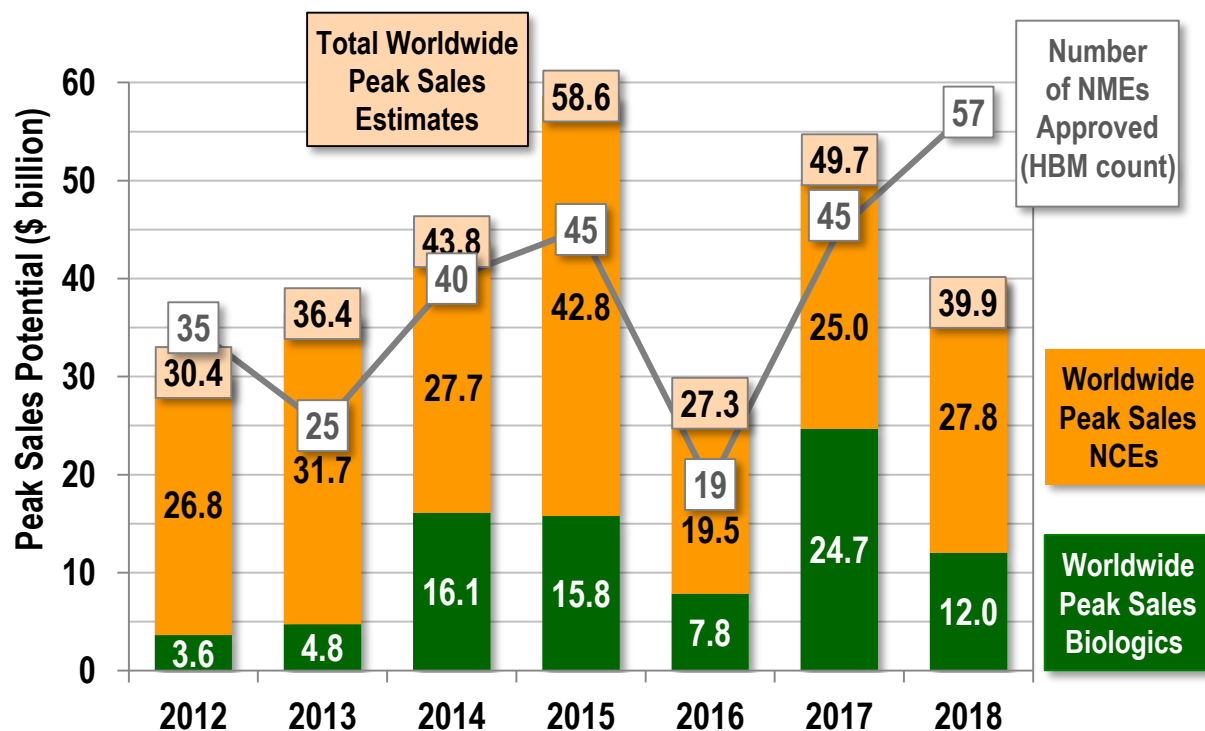
*NME approvals only

Estimated annual worldwide 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 become available.

Expected US peak sales 5 years after approval (a number frequently cited by some other sources such as EvaluatePharma) are about 50% lower than our worldwide peak sales estimates.

Are Small Molecule Drugs Making a Comeback?

Estimated Peak-Sales Potential of NCEs & Biologics Approved 2012-2018



Source: FDA, HBM Analysis / NME = new molecular entity / Biologics approved by CDER

Some new biologics - that can be considered NMEs - were approved by CBER (and not by CDER) and such products are not included in FDA's list of novel drugs and are also not included in our analysis.

For 2017, we estimated the market potential of such 6 products at \$5.2 billion.

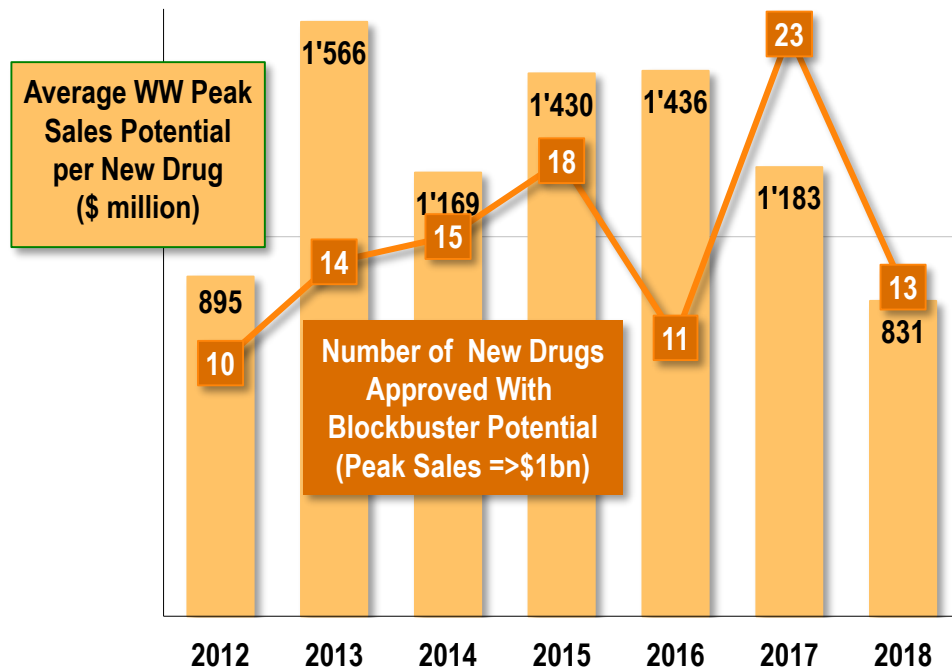
*In 2018, there were only 2 such products (**Jivi** and **Andexxa**) with a combined peak sales potential of \$1.2 billion.*

The 40 "traditional" small molecule drugs (NCEs) approved in 2018 are expected to generate \$27.8 billion in worldwide sales.

Peak sales potential of the 17 biologics approved in 2018 dropped to \$12 billion, even though there was a record number (17) of biologics approvals.

Fewer Potential Blockbusters Approved in 2018

Average Peak Sales Potential of New Drugs Approved 2012-2018



Source: FDA, HBM Analysis

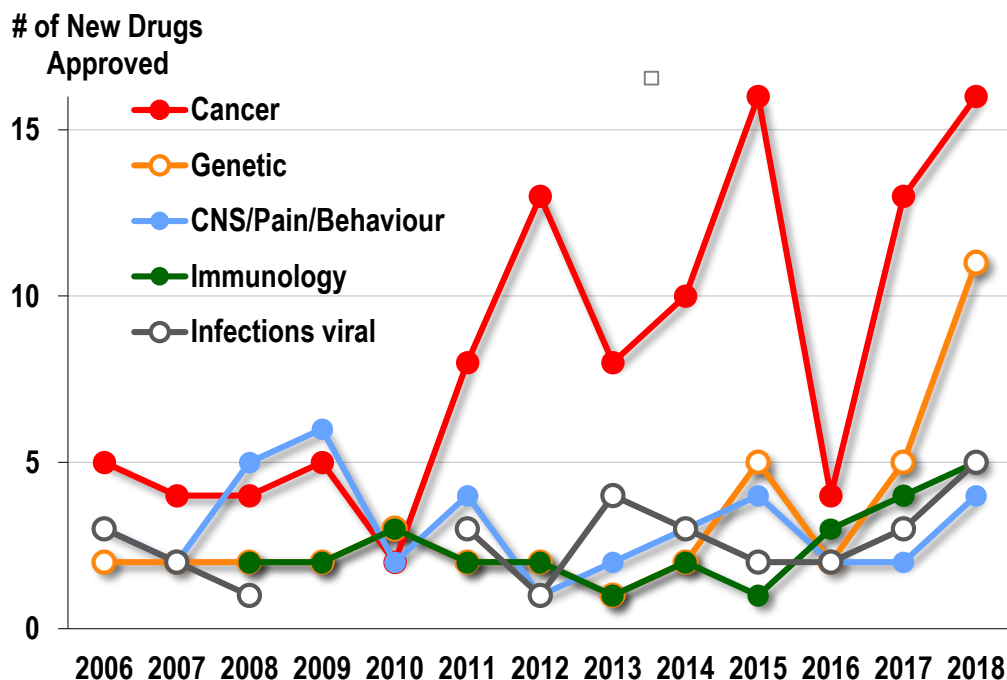
- Average peak sales potential of new drugs approved in 2018 dropped below \$1 billion.
- Only 13 potential new blockbuster drugs were approved in 2018 (as compared to 23 in 2017) ...
- ... with only 2 new potential blockbusters in oncology in 2018 (vs. 10 in 2017)!

New Drugs Approved in 2018 With Largest Peak Sales Potential

Drug (Company)	Peak Sales Potential \$ billion	Indication
Biktarvy (Gilead Sciences)	6.6	HIV
Ultomiris (Alexion)	2.3	Paroxysmal nocturnal hemoglobinuria (PNH)
Symdeko (Vertex Pharmaceuticals)	2.3	Cystic fibrosis
Orilissa (AbbVie)	1.9	Endometriosis
Crysvita (Ultragenyx)	1.8	X-linked hypophosphatemia (XLH)
Erleada (Johnson & Johnson)	1.7	Non-metastatic prostate cancer
Takhzyro (Shire)	1.7	Hereditary angioedema
Olumiant (Eli Lilly)	1.5	Moderate to severe rheumatoid arthritis
Epidiolex (GW Pharmaceuticals)	1.3	Dravet & Lennox-Gastau syndrome
Aimovig (Amgen)	1.3	Migraine
Libtayo (Regeneron Pharmaceuticals)	1.2	Metastatic cutaneous squamous cell carcinoma
Onpattro (Alnylam Pharmaceuticals)	1.1	Familial Amyloid Neuropathies
Lokelma (AstraZeneca)	1.0	Hyperkalemia

Cancer and Genetic Diseases with Most Approvals

New Drug Approvals 2006-2018 in Selected Therapeutic Areas



Since 2011, around 30% of approvals have been in oncology (as compared to approx. 20% in previous years).

11 new orphan drugs to treat rare genetic diseases were approved in 2018 with a total peak sales potential of almost \$10 billion!

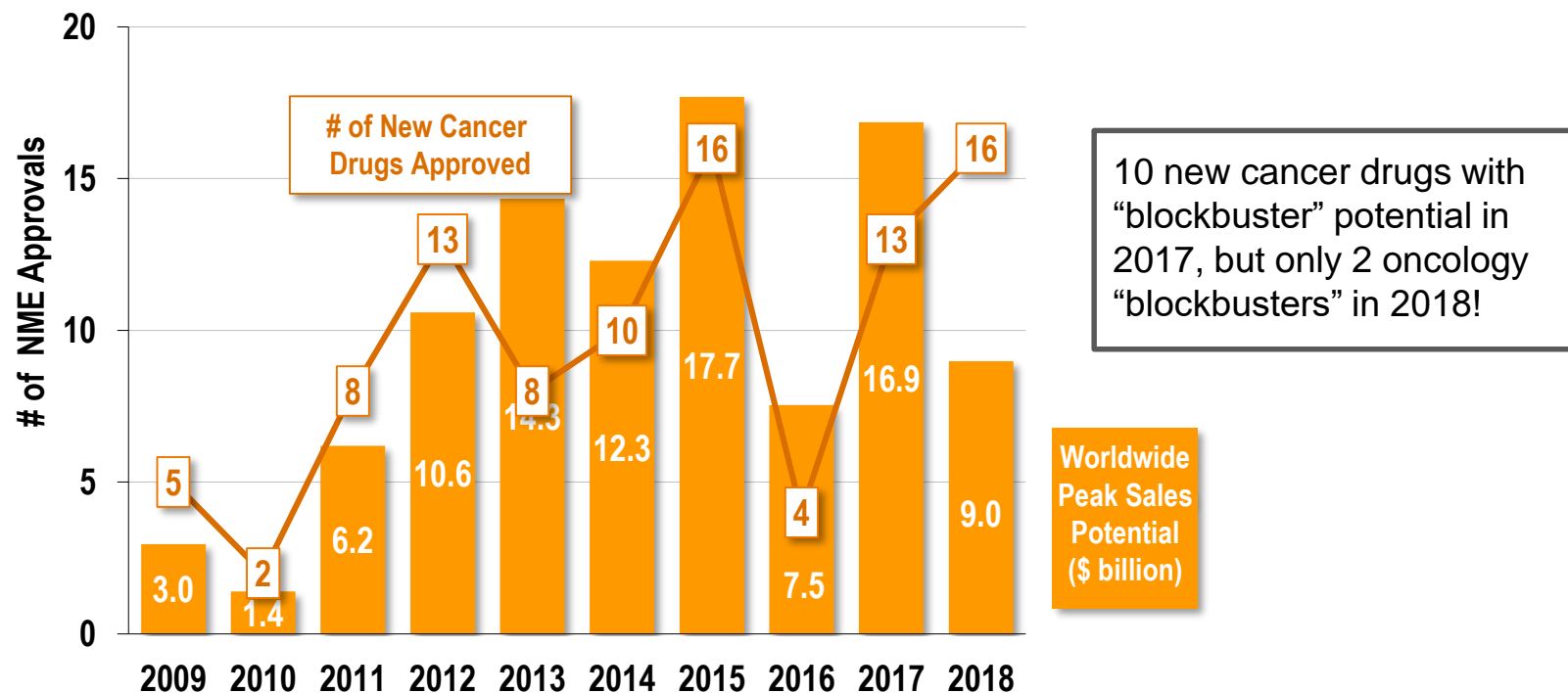
Anti-virals are a lucrative field for new drug development. Drugs in this area usually have a high sales potential.

- Highest number of new drug approvals in cancer (16) and rare genetic diseases (11, a new record!).
- Approval numbers in viral infections, CNS and immunology are also trending higher.

In 2018, 4 new antibiotics were approved (all with QIDP designation). The total market potential of these new drugs is rather modest (\$1.2 billion expected peak sales).

High Number of New Cancer Drug Approvals in 2018, But “Modest” Total Peak Sales Potential

New Drug Approvals in Oncology 2009-2018

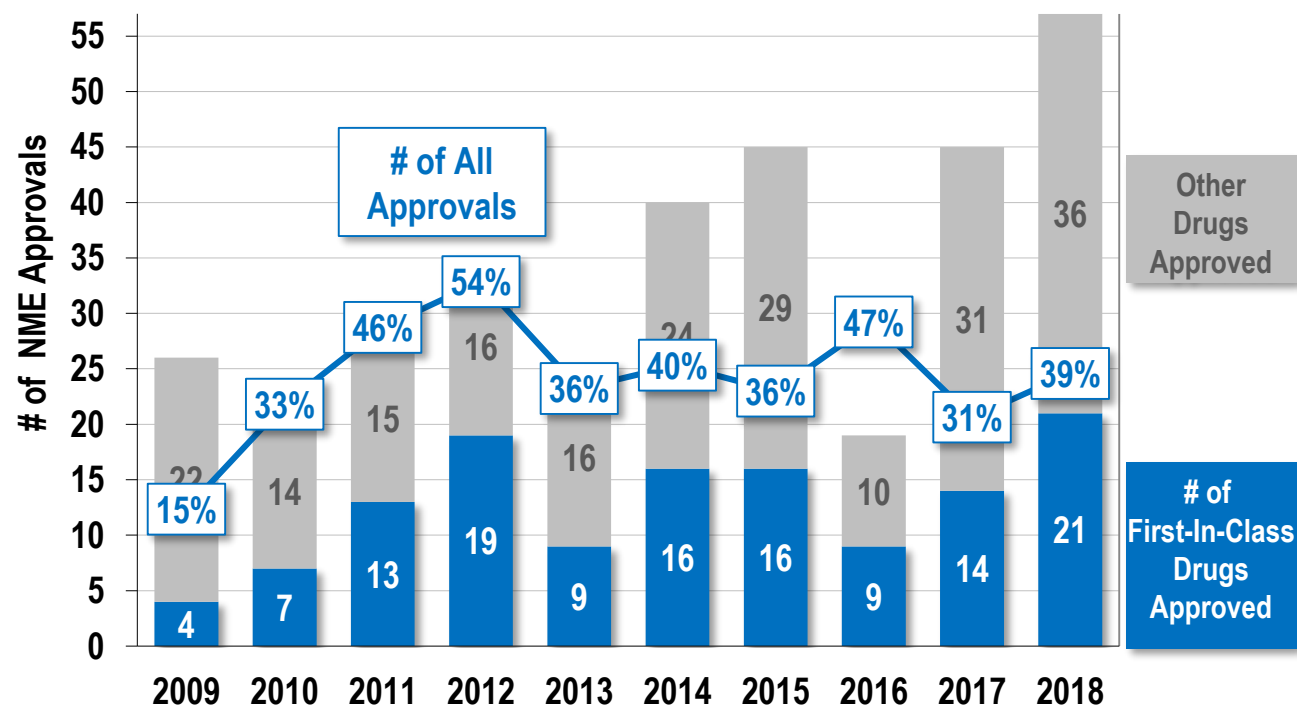


Source: FDA, HBM Analysis

- Considering the high number of cancer drug approvals in 2018, potential revenues from these new drugs seems modest.
- The 16 new cancers drugs approved in 2018 amount to 28% of all drug approvals (in-line with 5-year average).

The High Number of “First-in-Class” Drugs Approved in 2018 Indicate that Biopharma is Focussing on “True Innovations”

New First-in-Class Drugs Approved 2009-2018



Source: FDA, HBM Analysis

First-in-class drugs are “drugs which use a new and unique mechanism of action for treating a medical condition” (FDA definition).

The number of new first-in-class drugs approved is often used as an indicator of true innovation in pharma.

For 2018, FDA lists 20 new first-in-class drugs. Including Epidiolex, the first active ingredient derived from marijuana, generally considered a “first-in-class” drug by the industry, we count 21 new first-in-class drugs in 2018.

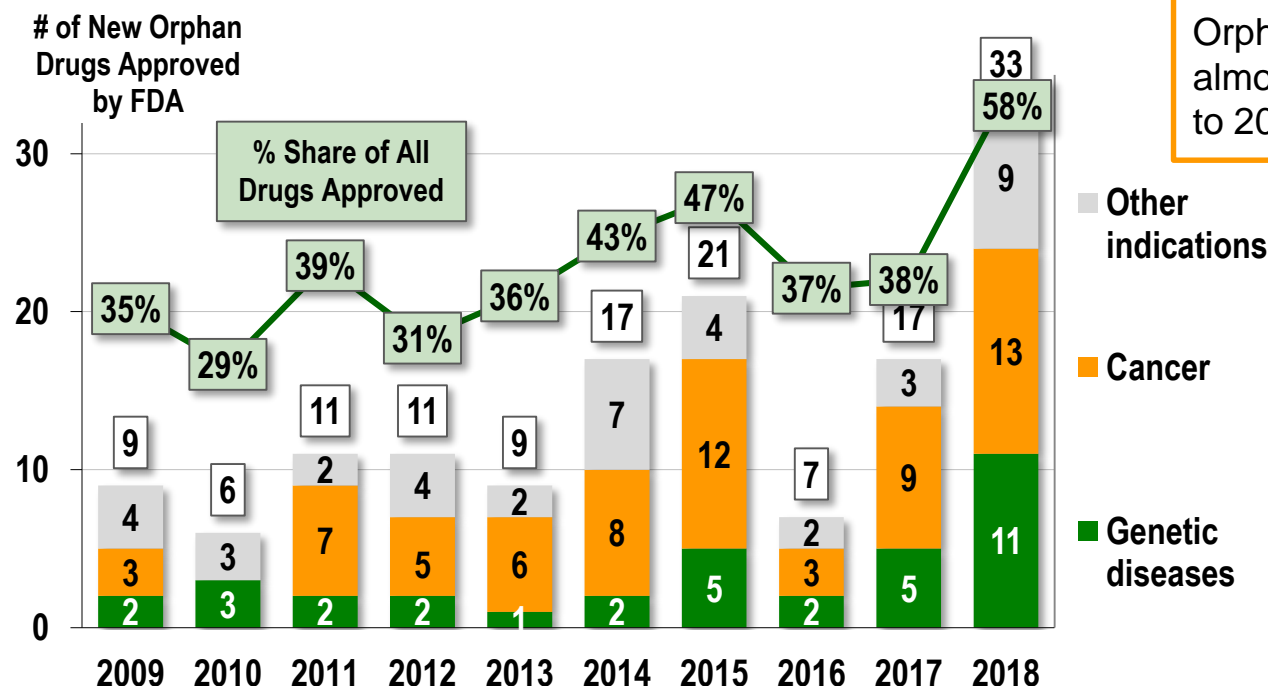
“USA First”:

42 of the 59* novel drugs approved in 2018 (71%) were approved in the US before getting approval in any other country.

* FDA count

Strong Increase in Orphan Drug Approvals since 2009

New Orphan Drugs Approved by FDA 2009-2019



Orphan drug approvals almost doubled from 2017 to 2018 (from 17 to 33)!

Orphan drugs have (on average) a somewhat lower peak sales potential than other (non-orphan) drugs.

Still high prices paid for genetic and other orphan disease treatments, quite a number of orphan drugs have “block-buster” potential.

Orphan cancer drugs are often expanded into larger indications thus leading to substantial additional revenues.

Source: FDA, HBM Analysis

Note: Some other products approved by CBER also had Orphan Designation

New Orphan Drugs Approved 2014-2018 with Blockbuster Potential

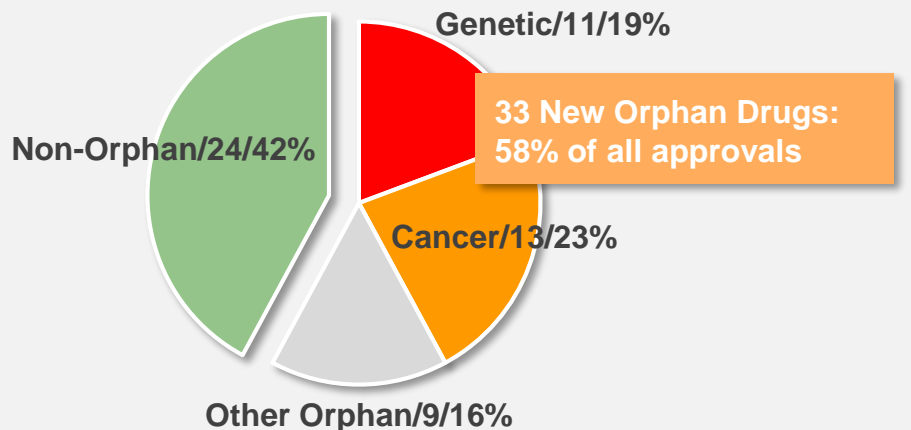
Average Peak Sales Potential 2014-18

	2014	2015	2016	2017	2018	2014-18	\$ billion
All Orphan Drugs	7	8	3	5	6	29	1.01
Cancer	4	4	1	4	-	13	0.97
Genetic	-	2	1	-	5	8	1.05
Other Indications	3	2	1	1	1	8	1.05

In 2018, 58% of New Drugs Approved Had “Orphan Drug Designation”

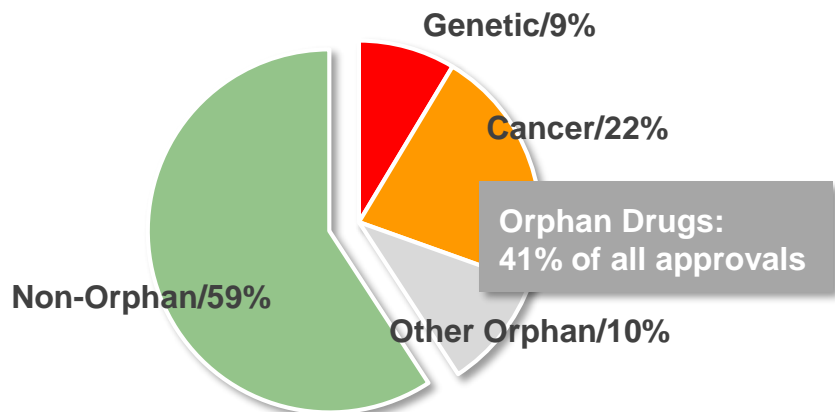
(as compared to approx. 40% in the years before)

Orphan Drug Approvals in 2018 ... (as % of all approvals)



Legend: Drug category or indication / Number of approvals / % of all approvals

... and for years 2013-2017



Legend: Drug category / % of all approvals

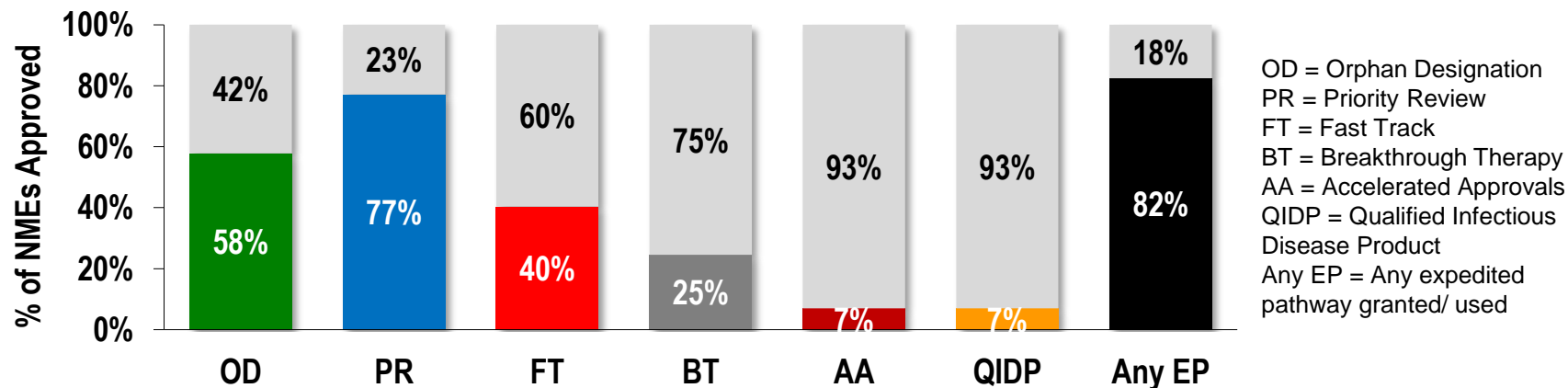
Companies with Highest Number of Orphan Drug Approvals 2009-2018

Company	# of Orphan Drug Approvals
Novartis	7
Pfizer	7
Roche	6
Johnson & Johnson	5
Bristol-Myers Squibb	5
AstraZeneca	5
Shire	4
GlaxoSmithKline	4
Alexion	3
Biomarin	3
Vertex Pharmaceuticals	3
Eli Lilly	3
Boehringer Ingelheim	3

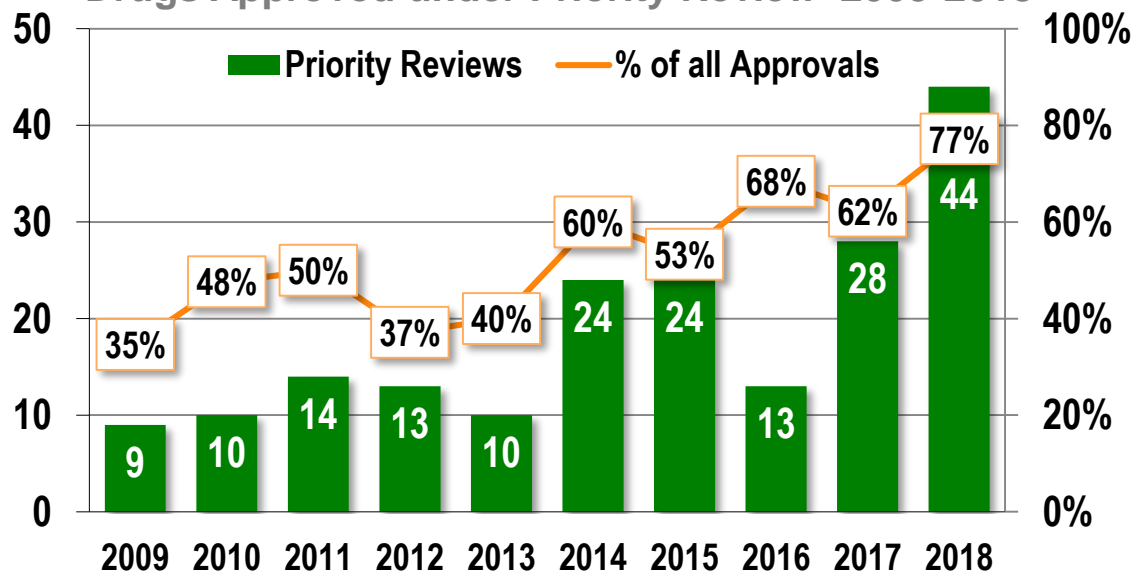
Companies outside of the
largest pharma companies

Over 80% of Drugs Approved in 2018 Took Advantage of Some Expedited Pathway (Priority Review, Fast Track etc.)

Drugs Approved in 2018 Using Expedited Pathways (% of all approvals)



Drugs Approved under Priority Review 2009-2018

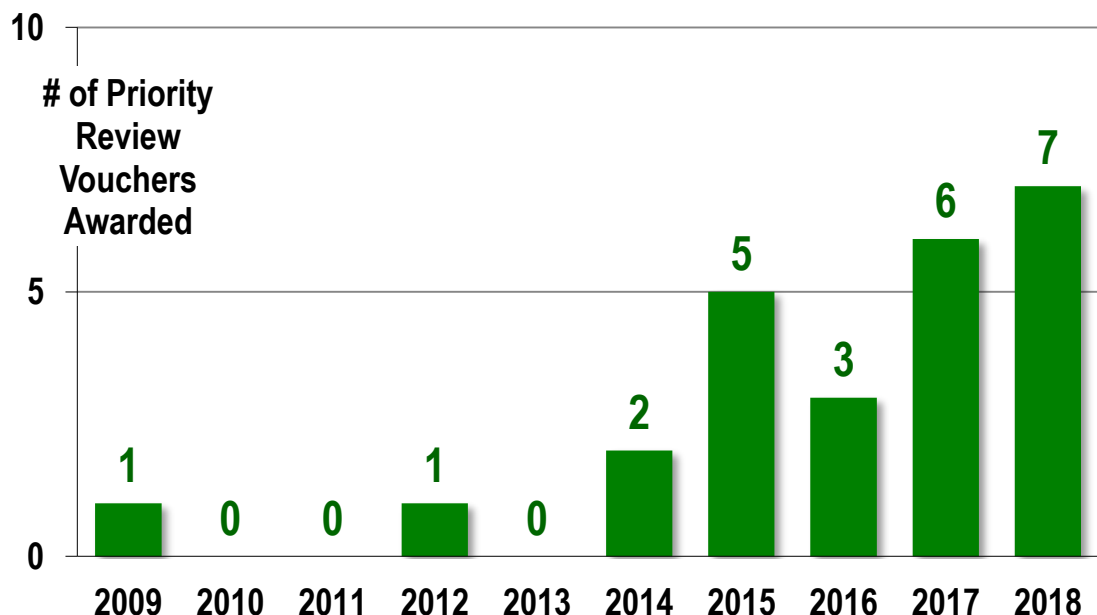


Significant increases seen in approvals with Priority Review, Fast Track, Breakthrough Therapy and Orphan Designation (both in absolute numbers and % of all approvals).

In 2018, only 4 drugs were granted Accelerated Approval (vs. 6 each in 2015, 2016 and 2017)

Highest Number of Priority Review Vouchers Awarded in 2018

Priority Review Vouchers (PRVs) Awarded 2009-2018



Includes PRVs awarded for new drugs/treatments approved by CDER and CBER.

Source: FDA, www.priorityreviewvoucher.org

11 PRVs were sold (so far) to other companies. Average PRV transaction values have come down to around \$80 million.

Considering that a significant number of PRVs are still unused, we do not expect a recovery of PRV values.

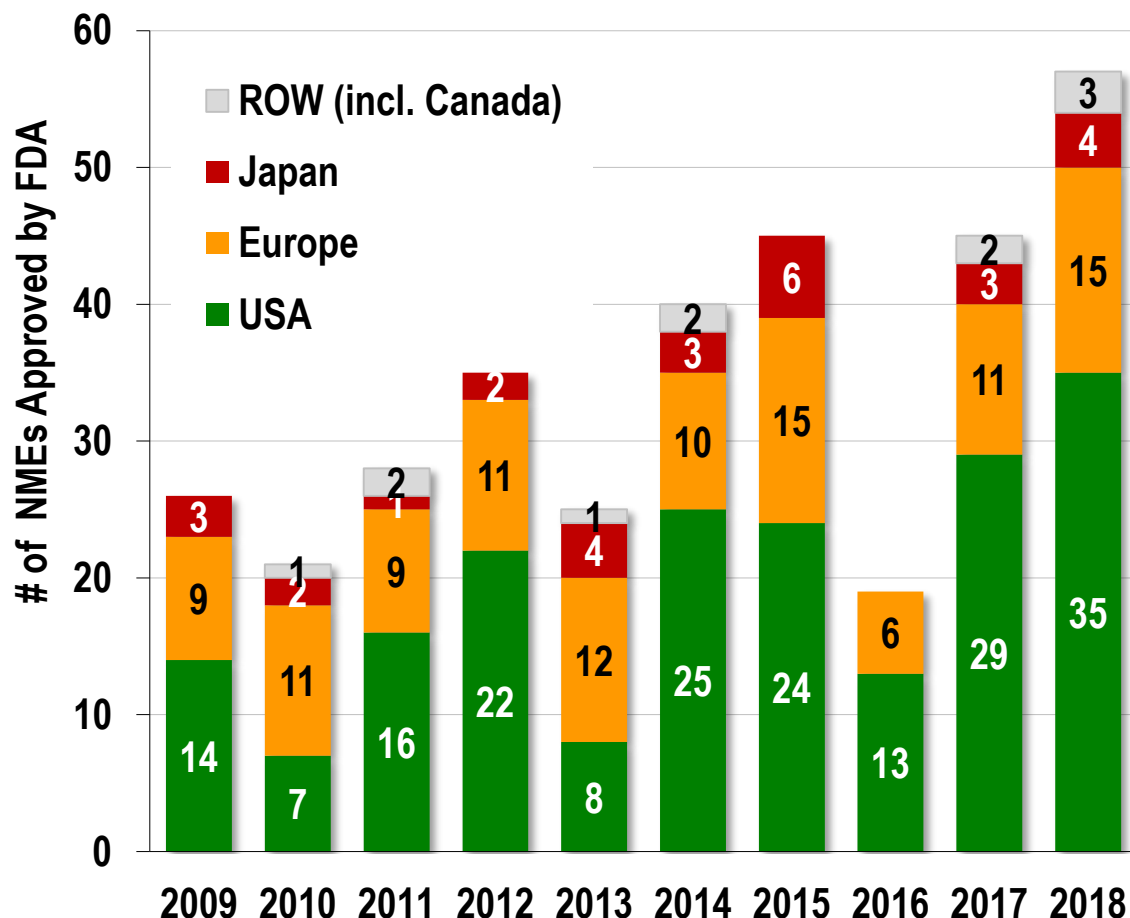
The Priority Review Voucher (PRV) Program was established in 2007.

Until the end of 2018 25 PRVs were awarded:

- 18 for rare pediatric diseases,
- 6 for neglected tropical diseases and
- 1 as a “Material Threat Medical Countermeasure” priority review voucher (TPOXX).

US and European Pharma Companies Still Dominate US Drug Approvals

Drug Owner/Sponsor - Headquarters Location by Country/Region



Only very few new drugs approved were sponsored/ owned by “ROW companies” with most of them being Canadian companies.

In 2018, Australian-based Medicines Development (with Moxidectin), Indian-based Sun Pharma (with Ilumya) and Canadian-based Theratechnologies (with Trogarzo) got one product approved each.

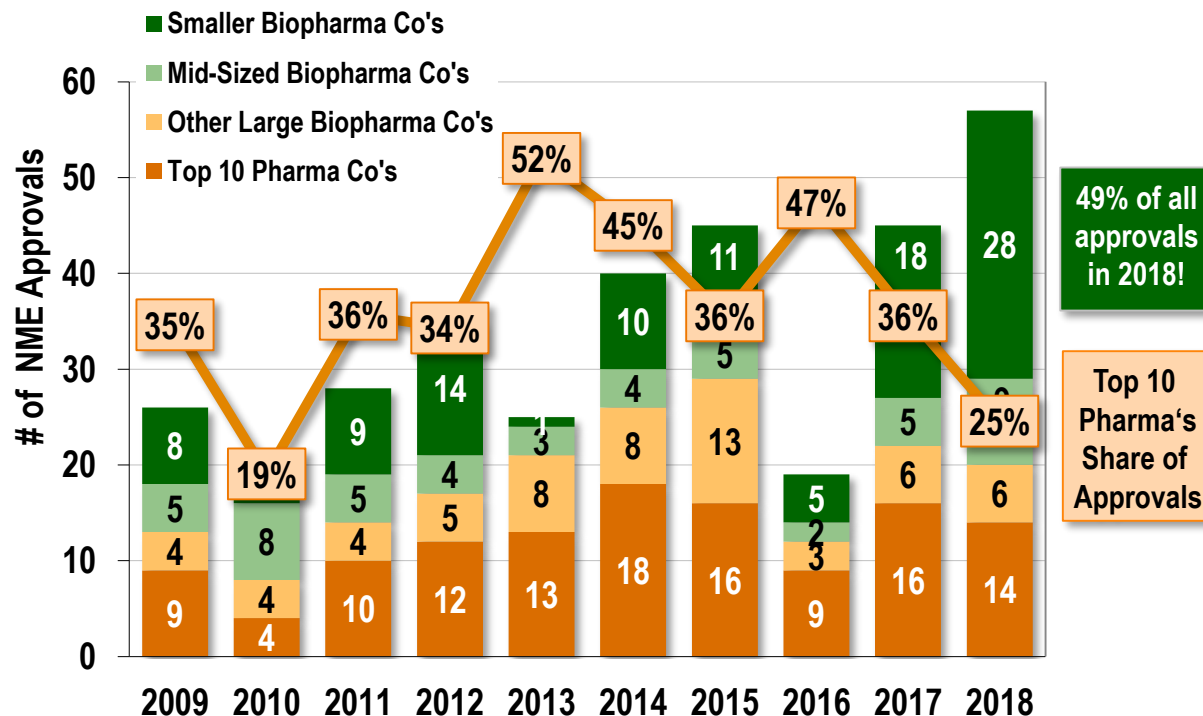
An analysis by the originators of new drugs shows an even stronger dominance by US companies: 40 of new drugs approved in 2018 were initially developed by US companies.

Source: FDA, HBM Analysis

Drug Owner/Sponsor = Company that owned drug at time of approval (or had US marketing rights)

Top 10 Pharma's Share of New Drug Approvals Declining, More Drugs from Smaller/Emerging Companies Get Approved

Drug Approvals by Types of Drug Owner/Sponsors



Source: FDA, HBM Analysis

- The share of new drug approvals of the Top 10 pharma companies has declined in recent years.
- Smaller biopharma companies (definitions see box on the right) are playing an increasing role not only as originators, but also as developers and owners of drugs all the way to approval.

Definitions:

The "Drug Sponsor/Owner" is the company that owns the drug at time of approval or has licensed it for US or worldwide markets

"Top 10 pharma companies": Pharma companies ranked within the top ten worldwide by pharma sales.

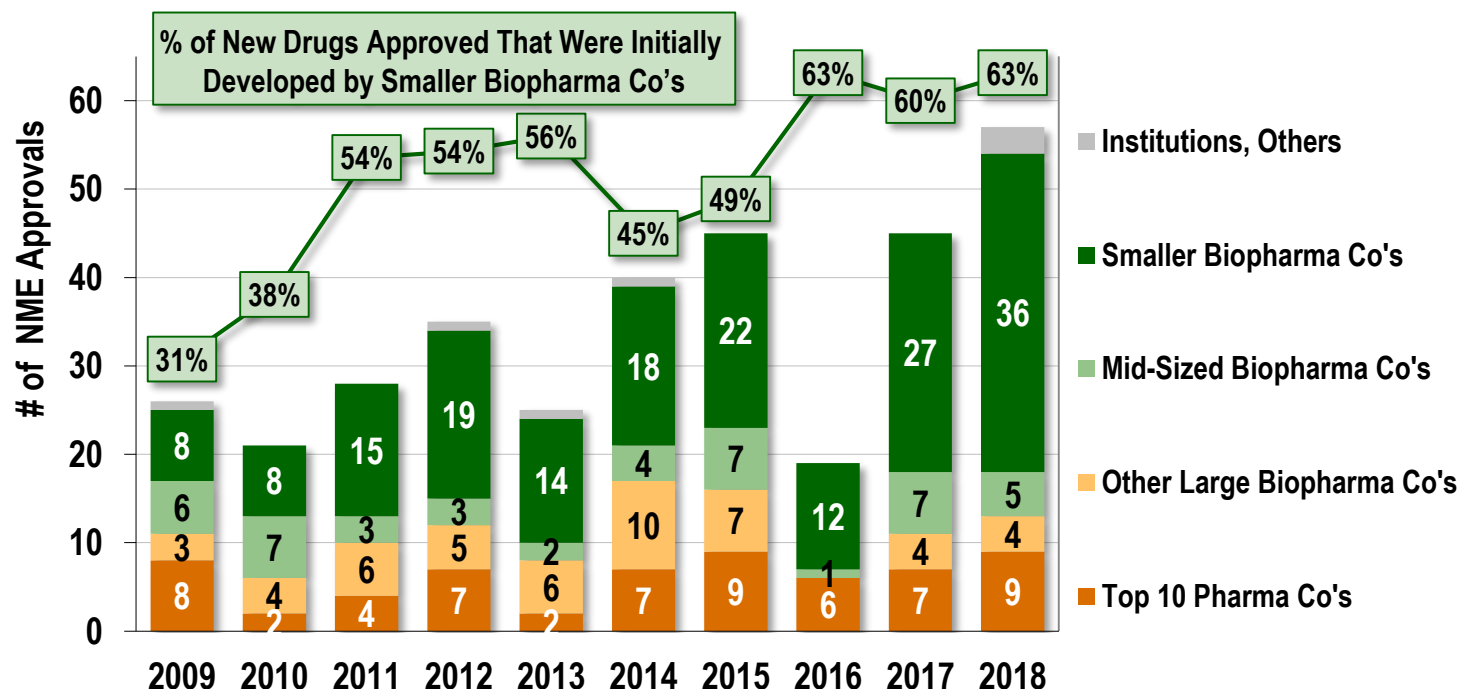
"Other large biopharma companies": Biopharma companies ranked between 11 and 30 in terms of worldwide sales.

"Mid-sized biopharma companies": Companies with significant sales of usually between \$100 million and \$1 billion.

"Smaller biopharma companies": = Other smaller biopharma companies.

The Majority of New Drugs Approved Originated at or Were Initially Developed by Smaller Biopharma Companies

Drug Approvals by Size Drug Originator*



* The “**Drug Originator**” is the company that discovered the drug or undertook the first serious clinical development effort.

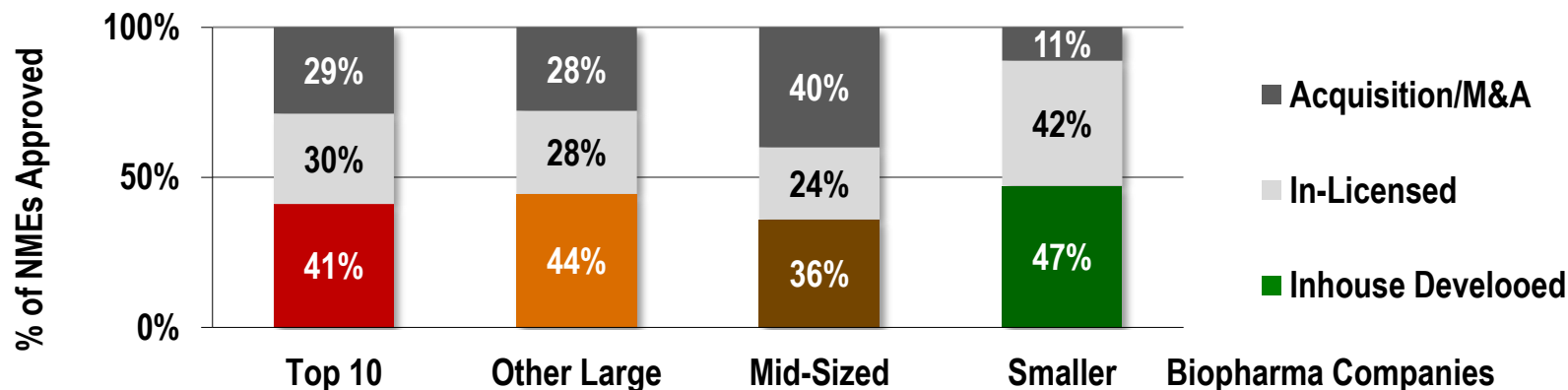
Note: A significant number of new drugs were originally discovered at universities or research institutions and then transferred to a biopharma company for initial or further development. We have listed such institutions only as “originators” if the transfer to a company occurred after pre-clinical development.

Source: FDA, HBM Analysis

- That small, innovative biopharma companies have been active in discovering and developing novel drugs is not a new phenomenon.
- In absolute and relative (%) terms, smaller companies now dominate the early development of new medicines.

Over 50% of New Drugs Approved Have Been In-licensed or Acquired

Origins of New Drugs Approved 2014-2018 By Type of Company (Drug Owner/Sponsor)

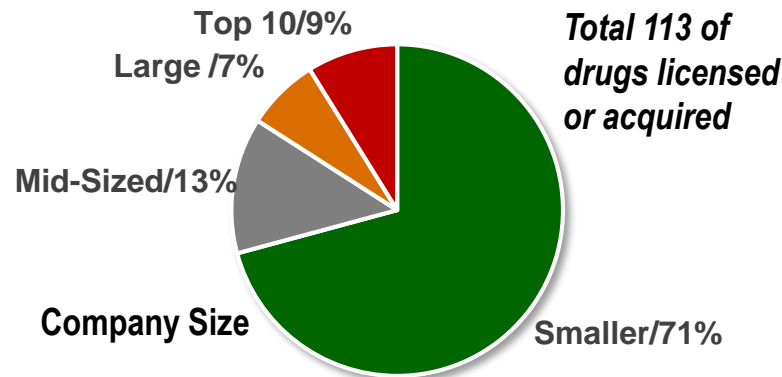


Source: FDA, HBM Analysis

Drug Owner/Sponsor = Company that owned drug at time of approval (or had US marketing rights)

Companies of all sizes use in-licensing and acquisitions to get access to novel drugs!

Origin of New Drugs Licensed or Acquired (Approved 2014-2019) by Company Sizes



113 drugs (54% of all that were approved 2014-18) "changed hands" before approval. 80 (or 71%) of those stem from smaller biopharma companies (50/50 licensing vs. trade sales).

HBM New Drug Approval Report - Notes

Which data is in the report (and which is not)?

The data for new drugs approved has been collected from FDA (www.fda.gov) and other sources.

The term “new drug” in this report is used for therapeutic new molecular entities (“NMEs”). This includes new chemical entities “NCEs” (also called small molecules) and new biologics such as antibodies etc. (classified by FDA as NMEs and approved by CDER).

Our data does not include FDA approvals for (a) new non-therapeutic agents such as imaging agents, preventive vaccines etc., some of which are included in FDA's older approval numbers and reports, (b) BLA approvals by CBER such as fractionated plasma products and other biologics products etc., (c) approvals of previously FDA-approved drugs for new indications, (d) new combinations or formulations of previously approved NMEs and (e) biosimilars.

In 2017 and 2018, we do provide data/information on selected BLAs approved by CBER for NME-like products, but products are not included in the analysis, graphs etc.

We thus follow the definition by the FDA for «Novel Drugs» (but exclude new imaging and other non-therapeutic agents, which were included mainly in earlier years by FDA).

**The use of data and charts is permitted with reference to
“HBM New Drug Approval Report”**

Further Reading

FDA 2018 New Drug Approval Report:

<https://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm592464.htm>

Fierce Biotech – List of new drugs approved in 2018 with some details:

<https://www.fiercebiotech.com/special-report/two-years-after-sluggish-2016-new-drug-approvals-hit-their-stride-2018>

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HBM Partners AG
Bundesplatz 1
CH-6300 Zug / Switzerland
Phone: +41 43 888 71 71
www.hbmpartners.com