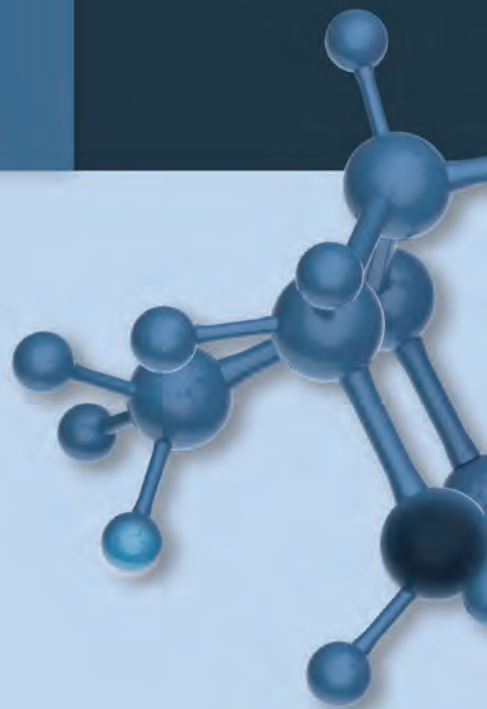


APPROVED DRUGS

2013

Adempas  
Anoro Ellipta  
Aptiom  
Breo Ellipta  
Brintellix  
Dotarem  
Duavee  
Gazyva  
Gilotrif  
Imbruvica  
Invokana  
Kadcyla  
Kynamro  
Luzu  
Lymphoseek  
Mekinist  
Nesina  
Olysio  
Opsumit  
Osphena  
Pomalyst  
Sovaldi  
Tafinlar  
Tecfidera  
Tivicay  
Vizamyl  
Xofigo



U.S. Food and Drug Administration  
Center for Drug Evaluation and Research  
[www.fda.gov/drugs](http://www.fda.gov/drugs)



Impact  
Innovation  
Predictability  
Access

January 2014

Novel New Drugs

2013

S U M M A R Y



U.S. Food and Drug Administration  
Center for Drug Evaluation and Research  
[www.fda.gov/drugs](http://www.fda.gov/drugs)

# CDER's 2013 Novel New Drugs

## 27 novel new drugs in CY 2013:

In Calendar Year 2013, FDA's Center for Drug Evaluation and Research (CDER) approved 27 novel new medicines, known as new molecular entities (NMEs). For the purposes of this report, the term NME applies to novel new drugs approved under both New Drug Applications (NDAs) and Biologics License Applications (BLAs). The chart below lists CDER's 2013 NMEs.

In  
2013  
CDER approved  
27  
NMEs

NMEs are often innovative new products that serve previously unmet medical needs or otherwise significantly help to advance patient care and public health. However, in some cases, while categorized as novel for technical and/or administrative purposes, a particular NME may not necessarily offer unique clinical advantages over existing therapies. This report summarizes all NMEs of 2013, with an emphasis on those that offer new and innovative treatments to patients in need.

The dark blue bars in the chart to the right indicate the number of NMEs approved by CDER in each year of the past decade. CDER approved 27 NMEs in 2013, which is similar to average totals of other years from this time period. For instance from 2004 through 2012, CDER has averaged about 26 NME approvals per year. In 2012, CDER approved 39 NMEs, but this was an unusually high number compared to any other total in more than a decade.

## Applications for new approvals remain steady

The number of applications CDER has been receiving for NMEs has not been consistently and significantly increasing. The light blue portion of the graph to the right indicates the number of new NDA and BLA applications for NMEs CDER has filed over the last ten years. From 2004 through 2012, CDER filed an average of about 34 applications for NMEs per year. Although all applications submitted in 2013 had not yet been accepted for filing as of 12/31/13, CDER projects about 36 for 2013, which is consistent with previous years in this decade.

With a relatively steady number of applications coming in over time, it is noteworthy that FDA cannot expect a continuing upward trend for NME approvals until a sustained increase in the number of applications for NMEs submitted for approval is also demonstrated.

### CDER's NMEs of CY 2013: see pages 14 & 15 for what these drugs are used for.

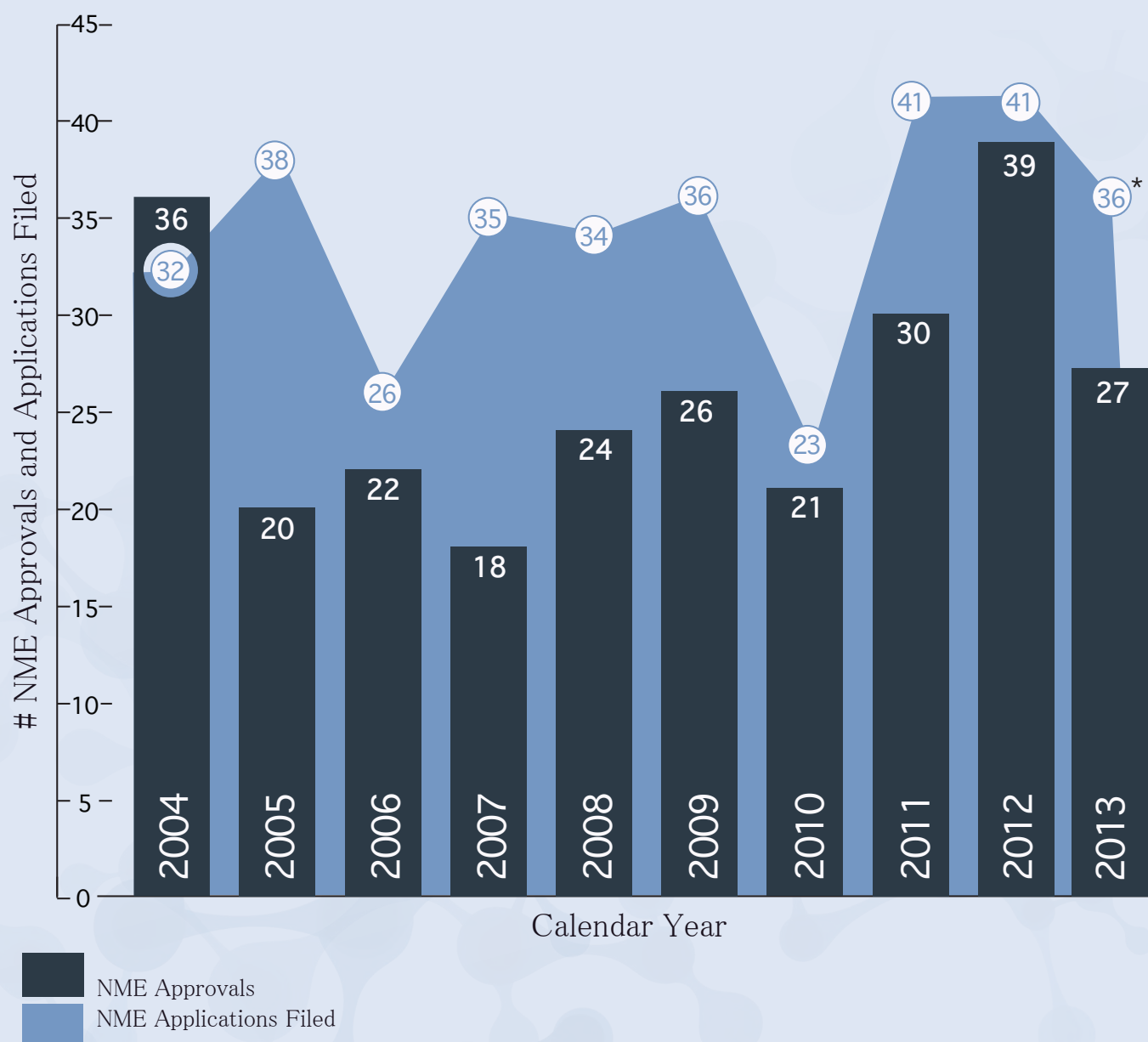
Adempas	Anoro Ellipta	Aptiom	Breo Ellipta	Brintellix	Dotarem	Duavee	Gazyva	Gilotrif
Imbruvica	Invokana	Kadcyla	Kynamro	Luzu	Lymphoseek	Mekinist	Nesina	Olysio
Opsumit	Osphena	Pomalyst	Sovaldi	Tafinlar	Tecfidera	Tivicay	Vizamyl	Xofigo

27 NMEs approved  
in CY 2013  
is similar to the  
average totals approved  
in the past decade

From 2004 through 2012,  
CDER has averaged

26

NME approvals per year



- \* - The filed numbers include those filed in CY 2013 plus those currently pending filing (i.e., within their 60 day filing period) in CY 2013.
- Receipts that received a "Refuse to File" (RTF) or "Withdrawn before filing" (WF) identifier are excluded.
  - Multiple submissions (multiple or split originals) pertaining to a single new molecular/biologic entity are only counted once.
  - There is a BLA included that does not currently have a review schedule but is known to contain a new active ingredient.
  - The filed number is not indicative of workload in the PDUFA V Program.



# Impact

## Impact on Public Health

Many of the 27 NMEs approved by CDER in CY 2013 are notable for their potential positive impact and unique contributions to quality care and public health.

### First-in-Class

Adempas

Imbruvica

Invokana

Kadcyla

Kynamro

Mekinist

Sovaldi

Tecfidera

Xofigo

One-third (33%) of the NMEs approved in CY 2013 (9 of 27) were identified by FDA as First-in-Class, meaning drugs which, for example, use a new and unique mechanism of action for treating a medical condition. First-in-Class is one indicator of the innovative nature of a drug and a 33% First-in-Class approval rate suggests that the group of CY 2013 NMEs is a field of innovative new products.

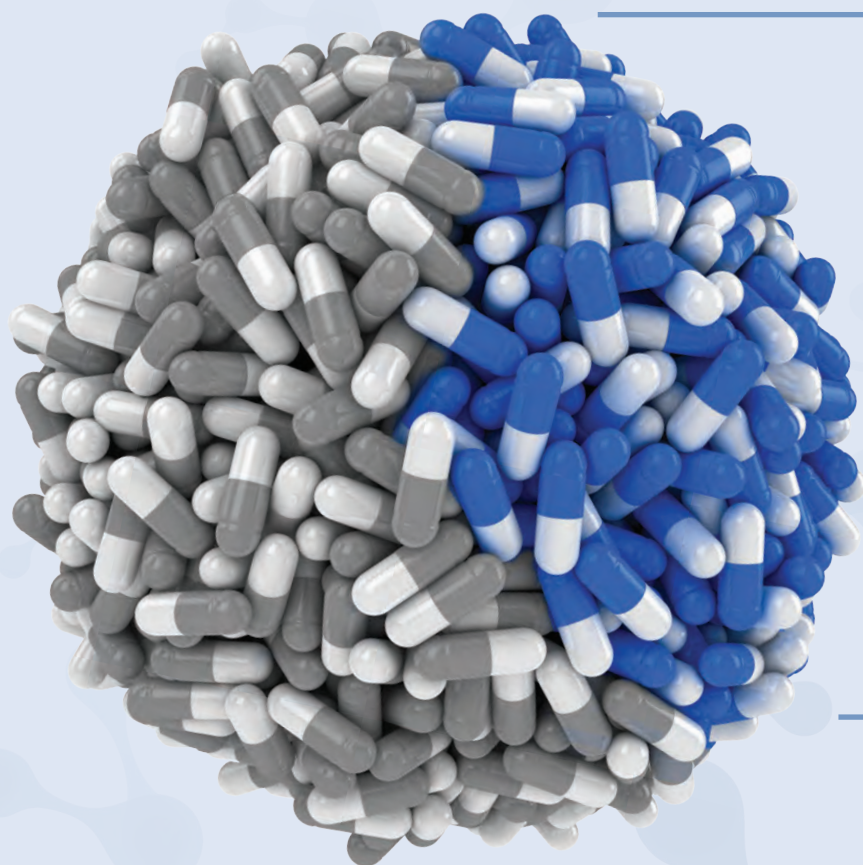
### Noteworthy First-in-Class products include:

**Invokana** - for type 2 diabetes glycemic control

**Kadcyla** - for HER2-positive late-stage (metastatic) breast cancer

**Sovaldi** - an interferon-free oral treatment option for some patients with chronic hepatitis C

**Mekinist** - for metastatic melanoma



33%  
First-in-Class  
Drugs

One-third (33%) of the NMEs approved in CY 2013 (9 of 27) were approved to treat rare or “orphan” diseases that affect 200,000 or fewer Americans. This is significant because patients with rare diseases often have few or no drug treatment options.

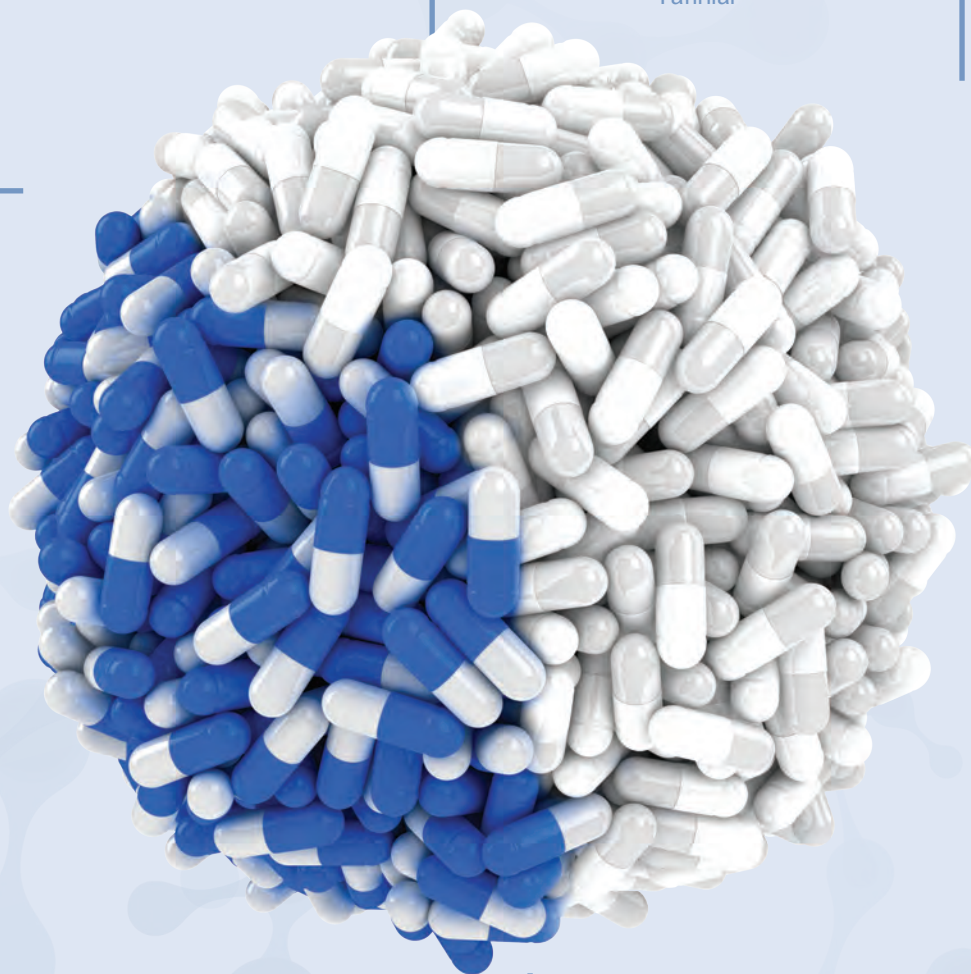
### Noteworthy examples of rare diseases that now have new or additional effective treatment options include:

Mantle cell lymphoma - *Imbruvica*  
Chronic lymphocytic leukemia - *Gazyva*  
Homozygous familial hypercholesterolemia - *Kynamro*  
Pulmonary arterial hypertension - *Adempas* and *Opsumit*

## Orphan Drugs

*Adempas*  
*Gazyva*  
*Gilotrif*  
*Imbruvica*  
*Kynamro*  
*Mekinist*  
*Opsumit*  
*Pomalyst*  
*Tafinlar*

33%  
Orphan Drugs



## Notable NMEs of 2013: Another strong year for quality

In addition to the nine noteworthy examples of innovative First-in-Class and “orphan” new products mentioned on pages 4 and 5, the 27 NMEs approved in CY 2013 also include Gilotrif to treat late stage (metastatic) non-small cell lung cancer, Tafinlar to treat patients with certain forms of melanoma, Tecfidera to treat adults with relapsing forms of multiple sclerosis, and Olysio for patients with chronic hepatitis C.

### Sovaldi

Treatment for patients with chronic hepatitis C.

### Olysio

Treatment for patients with chronic hepatitis C.

### Imbruvica

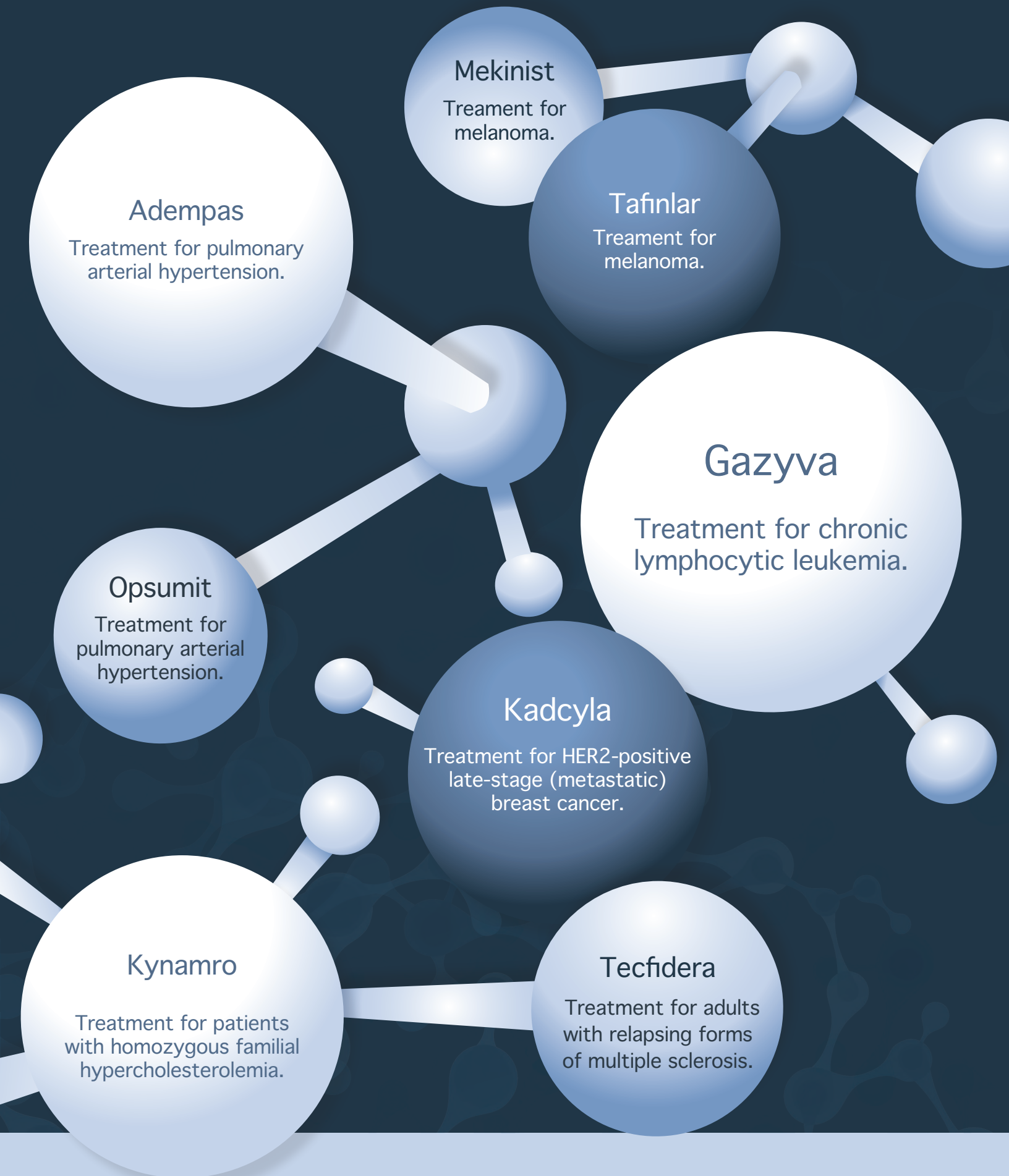
Treatment for mantle cell lymphoma.

### Invokana

Treatment for type 2 diabetes glycemic control.

### Gilotrif

Treatment for late stage (metastatic) non-small cell lung cancer.





# Innovation

## Innovative methods for expediting NMEs to market

Many of the 27 NMEs of CY 2013 approved by CDER are notable for the regulatory methods CDER used to expedite the development and approval process. From time of submission to their approval dates, some drugs were under review for only several months prior to approval. Particularly noteworthy examples of drugs approved rapidly are Gazyva approved in 6.3 months, Imbruvica approved in 4.5 months, and Xofigo approved in 5.0 months, all approved earlier than their goal dates for regulatory action. There are four FDA expedited review and approval pathways: Fast Track, Breakthrough, Priority Review, and Accelerated Approval.

### Fast Track

Gilotrif	Pomalyst
Imbruvica	Sovaldi
Kadcyla	Tafinlar
Mekinist	Tivicay
Olysio	Xofigo

Ten of the 27 NMEs approved in 2013 (37%) were designated by CDER as Fast Track, meaning drugs with the potential to address unmet medical needs. Fast Track speeds new drug development and review, for instance, by increasing the level of communication FDA allocates to developers and by enabling developers to use a “rolling review” process such that CDER can review portions of an application ahead of the submission of the full application.

Three of the 27 NMEs approved in 2013 (11%) were designated by CDER as Breakthrough therapies, meaning drugs with preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy. A breakthrough therapy designation conveys all of the fast track program features, as well as more intensive FDA guidance on an efficient drug development program. Breakthrough status is designed to help shorten the development time of a promising new therapy. This is a new designation that went into effect after July 9, 2012. 2013 is the first year any new drug was approved with the breakthrough designation.

### Breakthrough

Gazyva  
Imbruvica  
Sovaldi

### Priority Review

Adempas	Kadcyla
Dotarem	Olysio
Gazyva	Sovaldi
Gilotrif	Tivicay
Imbruvica	Xofigo

Ten of the 27 NMEs approved in 2013 (37%) were designated Priority Review, in which CDER determines the drug to potentially provide a significant advance in medical care and sets a target to review the drug within six months instead of the standard 10 months.

Two of the 27 NMEs approved in 2013 (7%) were approved under FDA's Accelerated Approval program, which allows early approval of a drug for serious or life-threatening illness that offers a benefit over current treatments. This approval is based on a “surrogate endpoint” (e.g., a laboratory measure) or other clinical measure that FDA considers reasonably likely to predict clinical benefit. After this approval, the drug must undergo additional testing to confirm that benefit; this speeds the availability of the drug.

### Accelerated Approval

Imbruvica  
Pomalyst

## Combined expedited approval methods

Drugs are not limited to one expedited development and approval method. In many cases, CDER uses one or more of these tools to speed development and approval. Almost half (48%) of the 27 NMEs approved in CY 2013 (13 of 27) were designated in one or more categories of Fast Track, Breakthrough, Priority Review, and/or Accelerated Approval. Each of these designations helps expedite the speed of the development and/or approval process and is designed to help bring important medications to the market as quickly as possible.

### Combined

Adempas	Imbruvica	Olysio	Tafinlar
Dotarem	Kadcyla	Pomalyst	Tivicay
Gazyva	Mekinist	Sovaldi	Xofigo
Gilotrif			



48%

Fast Track

37%

Breakthrough

11%

Priority Review

37%

Accelerated  
Approval

7%



# Predictability

Under the Prescription Drug User Fee Act (PDUFA), sponsors are assessed user fees that provide FDA with the additional resources needed to meet performance goals.

Throughout the year, CDER was able to meet or exceed PDUFA goal dates for application review, agreed to with the pharmaceutical industry and approved by Congress. In CY 2013, CDER met its PDUFA goal dates for 100% of the NMEs approved in CY 2013.

## PDUFA Goal Dates Met

Adempas	Lymphoseek
Anoro Ellipta	Mekinist
Aptiom	Nesina
Breo Ellipta	Olysio
Brintellix	Opsumit
Dotarem	Osphena
Duavee	Pomalyst
Gazyva	Sovaldi
Gilotrif	Tafinlar
Imbruvica	Tecfidera
Invokana	Tivicay
Kadcyla	Vizamyl
Kynamro	Xofigo
Luzu	



100%

Percentage of PDUFA goal  
dates met in CY 2013  
for each NME.

# Access

CDER approved most drugs (24 of 27) on the “first cycle” of review (89%), meaning without requests for additional information that would delay approval and lead to another cycle of review.

89% First Cycle Approval

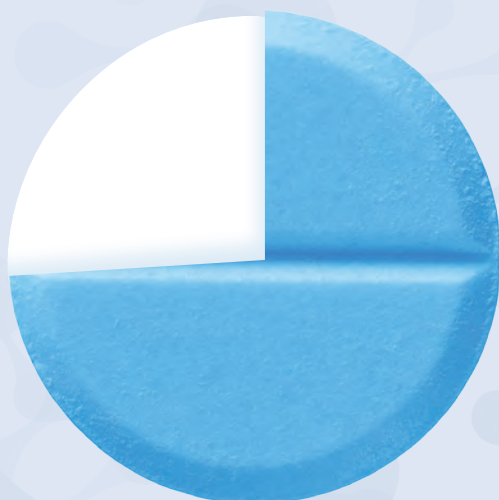
## First Cycle Approval

Adempas	Gazyva	Luzu	Sovaldi
Anoro Ellipta	Gilotrif	Mekinist	Tafinlar
Breo Ellipta	Imbruvica	Olysio	Tecfidera
Brintellix	Invokana	Opsumit	Tivicay
Dotarem	Kadcyla	Osphena	Vizamyl
Duavee	Kynamro	Pomalyst	Xofigo



Ten of the 24 First Cycle Approvals listed above are also designated as Priority Review drugs. This is particularly important because Priority Review drugs have the potential to serve as significant medical advances in health care.

74% First Approved in U.S.



## Approval in U.S. before Other Countries

Anoro Ellipta	Imbruvica	Mekinist	Tafinlar
Breo Ellipta	Invokana	Opsumit	Tecfidera
Brintellix	Kadcyla	Osphena	Tivicay
Gazyva	Kynamro	Pomalyst	Vizamyl
Gilotrif	Lymphoseek	Sovaldi	Xofigo

Comparing approval to other countries offers another measure of approval efficiency. Although regulatory processes differ widely between FDA and those of regulatory agencies in other countries, almost three-quarters (74%) of the NMEs approved in CY 2013 (20 of 27) were approved first in the U.S. before any other country.



# Overview

This document represents a broad overview of CDER approvals of new molecular entities (NMEs) for calendar year 2013.

A continuing upward trend for the annual number of CDER's NME approvals necessarily relies upon a corresponding upward trend in the number of applications submitted for approval. Over the past decade, submissions for NMEs by the pharmaceutical and biotechnology industry have not been increasing. In other words, over time, CDER can only approve a number of NMEs proportional to the number of applications for NMEs it receives.

More important than the quantity of new drugs approved in 2013 is the quality of the new drugs the pharmaceutical industry has developed and the important new roles these drugs are serving to advance medical care.

Also noteworthy is the efficiency with which most of these drugs were reviewed and approved. CDER used a variety of "expedited development and approval" regulatory tools to speed these drugs to market.

In all cases, while striving for efficiency of review and approval of applications for new drugs, CDER does not compromise its standards for demonstration of effectiveness and safety in the process.

More important than the quantity of new drugs approved by CDER in CY 2013 is the quality of the new drugs and the important new roles they are serving to advance medical care.

	First-in-Class	Orphan	Fast Track	Breakthrough	Priority Review	Accelerated Approval	Met PDUFA Goal Dates	First Cycle	First Approved in U.S.
Adempas									
Anoro Ellipta									
Aptiom									
Breo Ellipta									
Brintellix									
Dotarem									
Duavee									
Gazyva									
Gilotrif									
Imbruvica									
Invokana									
Kadcyla									
Kynamro									
Luzu									
Lymphoseek									
Mekinist									
Nesina									
Olysio									
Opsumit									
Osphena									
Pomalyst									
Sovaldi									
Tafinlar									
Tecfidera									
Tivicay									
Vizamyl									
Xofigo									

# Drug Designation Summary

## First-in-Class

Drugs with a new and unique mechanism for treating a medical condition.

## Orphan Drugs

Drugs approved for small populations of patients with rare diseases.

## Fast Track

Drugs that can treat unmet medical needs.

## Breakthrough

Drugs with preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy.

## Priority Review

A drug is given a priority review if there is potential to provide a significant advance in medical care.

## Accelerated Approval

Early approval based on markers that predict a reasonable benefit, with more testing to confirm clinical benefit after approval.

## PDUFA Goal Dates

Drugs that met the Prescription Drug User Fee Act goal dates for the year.

## First Cycle

Drugs that were approved without request for additional information that would delay approval and lead to another cycle of review.

## First Approved in U.S.

Drugs that were approved first in the U.S. before any other country worldwide.

# The NMEs of 2013

Drugs listed by date of approval.

Drug Name	Active Ingredient	Date	What it used for
<a href="#"><u>Nesina</u></a>	alogliptin	1/25/2013	To improve blood sugar control in adults with type 2 diabetes.
<a href="#"><u>Kynamro</u></a>	mipomersen sodium	1/29/2013	To treat patients with a rare type of high cholesterol called homozygous familial hypercholesterolemia (HoFH).
<a href="#"><u>Pomalyst</u></a>	pomalidomide	2/8/2013	To treat patients with multiple myeloma whose disease progressed after being treated with other cancer drugs.
<a href="#"><u>Kadcyla</u></a>	ado-trastuzumab emtansine	2/22/2013	For patients with HER2-positive, late-stage (metastatic) breast cancer.
<a href="#"><u>Osphena</u></a>	ospemifene	2/26/2013	To treat women experiencing moderate to severe dyspareunia (pain during sexual intercourse), a symptom of vulvar and vaginal atrophy due to menopause.
<a href="#"><u>Lymphoseek</u></a>	technetium Tc 99m tilmanocept	3/13/2013	A radioactive diagnostic imaging agent that helps doctors locate lymph nodes in patients with breast cancer or melanoma who are undergoing surgery to remove tumor-draining lymph nodes.
<a href="#"><u>Dotarem</u></a>	gadoterate meglumine	3/20/2013	For use in magnetic resonance imaging (MRI) of the brain, spine and associated tissues of patients ages 2 years and older.
<a href="#"><u>Tecfidera</u></a>	dimethyl fumarate	3/27/2013	To treat adults with relapsing forms of multiple sclerosis (MS).
<a href="#"><u>Invokana</u></a>	canagliflozin	3/29/2013	Used with diet and exercise to improve glycemic control in adults with type 2 diabetes.
<a href="#"><u>Breo Ellipta</u></a>	fluticasone furoate and vilanterol inhalation powder	5/10/2013	For the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.
<a href="#"><u>Xofigo</u></a>	radium Ra 223 dichloride	5/15/2013	To treat men with symptomatic late-stage (metastatic) castration-resistant prostate cancer that has spread to bones but not to other organs.
<a href="#"><u>Tafinlar</u></a>	dabrafenib	5/29/2013	To treat patients with melanoma whose tumors express the BRAF V600E gene mutation.
<a href="#"><u>Mekinist</u></a>	trametinib	5/29/2013	To treat patients whose tumors express the BRAF V600E or V600K gene mutations.
<a href="#"><u>Gilotrif</u></a>	afatinib	7/12/2013	For patients with late stage (metastatic) non-small cell lung cancer (NSCLC) whose tumors express specific types of epidermal growth factor receptor (EGFR) gene mutations, as detected by an FDA-approved test.

Drug Name	Active Ingredient	Date	What it used for
<u>Tivicay</u>	dolutegravir	8/12/2013	To treat HIV-1 infection.
<u>Brintellix</u>	vortioxetine	9/30/2013	To treat adults with major depressive disorder.
<u>Duavee</u>	conjugated estrogens/ bazedoxifene	10/3/2013	To treat moderate-to-severe hot flashes (vasomotor symptoms) associated with menopause and to prevent osteoporosis after menopause.
<u>Adempas</u>	riociguat	10/8/2013	To treat adults with two forms of pulmonary hypertension.
<u>Opsumit</u>	macitentan	10/18/2013	To treat adults with pulmonary arterial hypertension (PAH), a chronic, progressive and debilitating disease that can lead to death or the need for lung transplantation.
<u>Vizamyl</u>	flutemetamol F 18 injection	10/25/2013	A radioactive diagnostic drug for use with positron emission tomography (PET) imaging of the brain in adults being evaluated for Alzheimer's disease (AD) and dementia.
<u>Gazyva</u>	obinutuzumab	11/1/2013	For use in combination with chlorambucil to treat patients with previously untreated chronic lymphocytic leukemia (CLL).
<u>Aptiom</u>	eslicarbazepine acetate	11/8/2013	As an add-on medication to treat seizures associated with epilepsy.
<u>Imbruvica</u>	ibrutinib	11/13/2013	To treat patients with mantle cell lymphoma (MCL), a rare and aggressive type of blood cancer.
<u>Luzu</u>	luliconazole	11/14/2013	For the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms Trichophyton rubrum and Epidermophyton floccosum in patients 18 years of age and older.
<u>Olysio</u>	simeprevir	11/22/2013	To treat chronic hepatitis C virus (HCV) infection.
<u>Sovaldi</u>	sofosbuvir	12/6/2013	To treat chronic hepatitis C virus (HCV) infection.
<u>Anoro Ellipta</u>	umeclidinium and vilanterol inhalation powder	12/18/2013	For the once-daily, long-term maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).