EvaluatePharma®

Orphan Drug Report 2018

5th Edition – May 2018

Evaluate®

Welcome to the EvaluatePharma® Orphan Drug Report 2018

The fifth edition of EvaluatePharma's Orphan Drug Report brings together analyses to provide top-level insight, from the world's financial markets, into the expected performance of the orphan drug market between now and 2024. Based on EvaluatePharma's coverage of over 7,000 of the world's leading pharmaceutical and biotech companies, the Orphan Drug Report 2018 highlights trends in prescription sales of orphan drugs, USA cost of treatment, leading products with an orphan drug designation, key companies in the rare diseases landscape and orphan drug designation analysis by region.

Additional copies are available at:
www.evaluategroup.com/OrphanDrug2018

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Overview

An orphan drug is a pharmaceutical product that treats a rare condition or disease. The development of orphan drugs has been financially incentivised through US law via the Orphan Drug Act of 1983. The National Organization for Rare Disorders (NORD), which was instrumental in establishing the Act, currently estimates that there are as many as 7,000 rare diseases and that up to 30 million Americans suffer from a rare disease. Prior to the 1983 Act, 38 orphan drugs were approved in the United States. The success of the original Orphan Drug Act in the USA led to it being adopted in other key markets, most notably in Japan in 1993 and in the European Union in 2000.

Rare disease patient populations are defined in law as:

- **USA:** <200,000 patients (<6.37 in 10,000, based on US population of 314m)
- **EU:** <5 in 10,000 (<250,000 patients, based on EU population of 514m)
- **Japan:** <50,000 patients (<4 in 10,000 based on Japan population of 128m)

Financial incentives by law include:

Orphan drug exclusivity

During the period of marketing exclusivity, the regulatory bodies are barred from approving the same product for the same orphan indication. A product holding several separate orphan designations for different indications can have several separate market exclusivities, which can run concurrently.

- **USA:** Seven years of marketing exclusivity from approval.
- **EU:** Ten years of marketing exclusivity from approval.
- **Japan:** Ten years registration validity period (also known as re-examination period).

Reduced R&D costs

- **USA:** 50% Tax Credit on R&D Cost (owing to new tax legislation, is expected to decrease to 25%).
- **USA:** R&D Grants for Phase I to Phase III Clinical Trials.
- **USA:** User fees waived (FFDCA Section 526: Company WW Revenues <$50m).
- **EU:** EMA protocol assistance at a reduced cost.
- **EU:** Administrative and procedural assistance at a reduced fee for small and medium sized enterprises.
- **EU:** The EMA does not offer research grants but funding is available for the European Commission (EC) and other sources, such as Horizon 2020 and E-Rare.
- **Japan:** Orphan products can be subsidised through the National Institute of Biomedical Innovation (NIBIO).
- **Japan:** Guidance and consultations from the Pharmaceuticals and Medical Devices Agency (PMDA) at a lower user fee.
- **Japan:** 12% of study expenses incurred during the NIBIO payment period can be reported as a tax credit.

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Overview

Orphan drug classification methodology

EvaluatePharma have identified all products that have orphan drug designations filed in the USA, EU or Japan.

These are available as part of the core EvaluatePharma service. To further enhance analysis, EvaluatePharma have defined an 'Orphan' sub-set of products using these criteria:

- Initial approval in the USA, EU or Japan was for a rare disease for which the product had orphan designation.
- Products not initially approved for treatment of an orphan indication, expected to generate more than 50% of sales from use in orphan indications. This has led to the exclusion of drugs such as Avastin, Enbrel, Herceptin, Humira and Remicade, all of which have orphan designations for indications contributing less than 50% of sales.
- Indication – the product is being examined in an indication that is classified as an orphan disease in and for which other products approved in this indication were also approved as orphan drugs.
- Company news – the company developing the product states it is seeking orphan drug designation for it's lead indication.

All sales analysis in the report is based on this 'Orphan' sub-set of products. Product sales represent total brand sales.

Prices for products in the US are sourced from Medicare Part B, National Average Drug Acquisition Cost (NADAC), Federal Supply Schedule (FSS) and Medicaid.

Availability of a price point determines choice of source. The source is kept consistent across years to reflect a clear trend in pricing.

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Foreword

The unmet medical needs of some of the sickest patients in society have pretty much guaranteed any developer working in the field of orphan drugs would be handsomely rewarded for their efforts.

However, EvaluatePharma's fifth edition of the orphan drug report shows that although the overall market is growing strongly the year-on-year price increases orphan drugs can command have fallen.

This dip in the amount pharma companies are able to command for these rare disease products raises the question; has the pushback against orphan drug pricing begun?

The warning signs about orphan drug pricing started to appear last year, when both payers and politicians began to take a much closer look at these niche treatments. There was talk of abuses of the Orphan Drug Act and members of the US congress asked questions about the fairness of big pharma using the associated tax and regulatory advantages of developing orphan drugs.

The fact that this year's report shows that seven of the top 10 companies by orphan sales are still big pharma groups, will not help the ongoing debate as to whether these well-funded groups should be benefiting from the regulatory and commercial advantages associated with orphan drugs.

Although pricing may have taken a bit of a pounding this year, in absolute terms the orphan drug market is growing strongly.

> According to this year's report sales of orphan drugs are set to climb by 11% a year all the way through to 2024, eventually reaching $262bn – this compares with 6.4% growth for the overall pharma market in the same period.

Despite the slowdown in pricing, the mean cost per patient per year still managed to hit $147,308 in 2017, more than four times the mean cost for non-orphan drugs at $30,708.

In terms of the sector's biggest players, 2017 saw a significant reshuffle at the top, with Celgene toppling Novartis to take the crown as the company with the biggest orphan drug sales, thanks to Revlimid, which qualifies for orphan drug designation through its multiple myeloma indication.

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Foreword

Although the biggest company changed, Soliris retained its spot at the top as the sector's most expensive drug, as the annual price of the treatment for paroxysmal nocturnal haemoglobinuria tipped over $500,000. But, this is likely to be Soliris's last year as number one. In February, the FDA approved Biogen's Spinraza for spinal muscular atrophy, with a price tag of $750,000 in the first year of treatment, falling to $350,000 in the second. There is also BioMarin's Brineura for Batten disease, whose $27,000 biweekly injections add up to an annual list price of $702,000.

With payers already bristling at the cost of some of the newer orphan drugs on the market, the UK's NICE has already rejected Brineura for being too expensive, those developing even more expensive products, like gene therapies, might find even tougher hurdles to reimbursement. Spark Therapeuticsrecently priced its retinal dystrophy gene therapy product, Luxturna at $850,000.

A recent survey by the Pharmacy Benefit Management Institute showed that cost is the primaryconcern for 55% of payers, and 71% do not believe that current prices are sustainable.

As such it will be difficult to predict the market impact of these types of innovation that will test existing payment models to their limits. Evaluate is taking a keen interest in this and orientating its industry content around these disruptive evolutions in the landscape.

However, pricing pressure might not be the only future brake on the growth of the rare disease sector. The recent US tax reform legislation, that gave big pharma their much vaunted tax holiday, alsoslashed the tax credit for orphan drug developers from 50% to 25%.

As such, the orphan drug market is at an interesting crossroads in its development. On the one hand with the cost of development set to rise and increasing payer pushback, the sector could become less attractive for both smaller and larger companies. Glaxosmithkline and Astrazeneca have already announced their intentions to withdraw from the space.

On the other hand there are still thousands of orphan conditions that remain untouched by medical innovation, making it an area still ripe with opportunity. But if the orphan drug sector is to achieve the growth targets ascribed to it, the trick will be to getting products to patients in the most efficient and cost effective way

Report Author:
Karen Pomeranz, PhD
Managing Analyst, EvaluatePharma
karen.pomeranz@evaluategroup.com

Foreword by:
Lisa Urquhart
Editor, EP Vantage
lisau@epvantage.com

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Analysis Highlights

- Worldwide orphan drug sales are forecast to grow at a CAGR of 11.3% from 2018 to 2024, double the rate forecast for the non-orphan drug market.
- By 2024, orphan drugs are expected to capture a fifth of worldwide prescription sales and to reach $262bn.

- The mean price of the top 100 USA orphan drugs (ranked by sales) grew at an annual rate of 5.2% from 2013 to 2017 compared to 9.2% for the top 100 non-orphan drugs.
- Revlimid (lenalidomide) is forecasted to be the top selling orphan drug in the USA, in 2024.
- Soliris (eculizumab) was the highest revenue generating orphan drug, per patient in the USA, in 2017.
- Expected strong sales of Revlimid and Pomalyst (pomalidomide) will secure Celgene's position as 2024 worldwide leader in orphan drug sales.
- Alexion Pharmaceuticals is the current worldwide leading company in the orphan drug market for blood indications.
- Oncology is the leading 2024 orphan drug therapy area accounting for about 50% of the total 2024 worldwide market. Blood is the second leading therapy area, accounting for about 12% of the market.
- Sales forecasts for pipeline orphan drugs account for over a third of total R&D pipeline sales through to 2024.
- Lanadelumab (Shire) is the most valuable R&D orphan drug with a NPV of $7.5bn.
- Implementation of the FDA's orphan drug modernization plan has led to an increase in the number of orphan designation granted in the USA. Overall, the FDA has granted more orphan drug designations than any other regulatory body.

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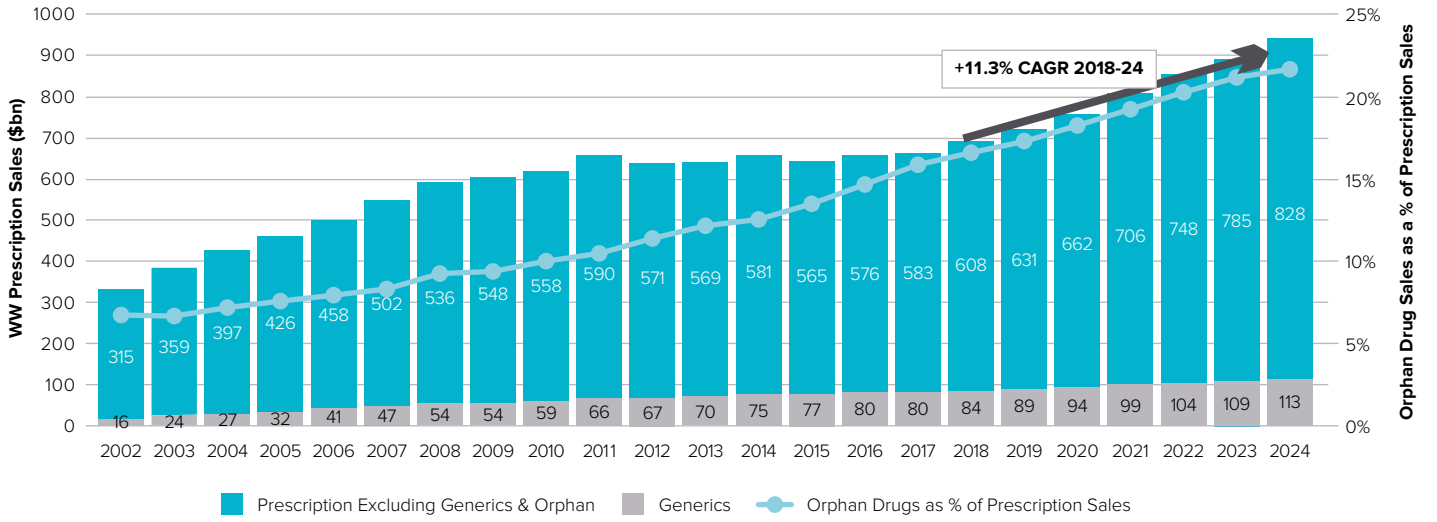
Worldwide Orphan Drug Sales (2002-2024)

Worldwide orphan drug sales forecast to total $262bn in 2024. The CAGR of orphan drugs between 2018 and 2024 forecast to be +11.3%, approximately double that of the non-orphan market. Orphan drugs set to be 21.7% of worldwide prescription sales by 2024.

EvaluatePharma® finds that sales of drugs designated as orphans will grow by 11% per year through to 2024, reaching $262bn. The growth of the orphan drug market is anticipated to be more than double that of the overall prescription drug market, with orphan drugs set to account for a little over a fifth of all prescription drug sales by 2024. This is in comparison to 2017, when orphan drugs held just a 16% share of the market. The rapid growth in the orphan drug market share mainly stems from sales of currently approved therapies and not from expected sales, through to 2024, of R&D products (see page 24).

Worldwide Orphan Drug Sales & Share of Prescription Drug Market (2002-2024)

Source: EvaluatePharma® May 2018



Worldwide Orphan & Prescription Drug Sales (2010-2024)

Source: EvaluatePharma® May 2018

	Worldwide sales ($bn)														
Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Orphan drug sales	69	77	82	88	94	100	112	125	138	151	169	192	216	240	262
Growth per year		+11.7%	+6.7%	+7.7%	+6.8%	+6.3%	+12.5%	+11.3%	+9.9%	+9.6%	+11.9%	+13.4%	+12.9%	+10.8%	+9.2%
Orphan sales as a % of Rx	10.0%	10.5%	11.4%	12.1%	12.5%	13.5%	14.6%	15.9%	16.6%	17.3%	18.3%	19.2%	20.2%	21.1%	21.7%
Non-orphan drug sales	618	656	638	639	657	642	655	663	692	720	756	805	852	893	941
Growth per year		+6.2%	-2.7%	+0.1%	+2.8%	-2.2%	+2.0%	+1.1%	+4.4%	+4.1%	+5.1%	+6.4%	+5.9%	+4.8%	+5.3%
Prescription (Rx) (excluding generics)	627	667	653	657	675	665	688	708	746	782	831	897	965	1,024	1,090
Growth per year		+6.3%	-2.0%	+0.6%	+2.8%	-1.5%	+3.4%	+2.9%	+5.3%	+4.9%	+6.3%	+8.0%	+7.5%	+6.2%	+6.4%

WW Orphan Drug Market CAGR 18-24 +11.3%
WW Non-Orphan Drug Market CAGR 18-24 +5.3%
WW Prescription (Rx) Excluding Generics CAGR 18-24 +6.5%

Note: Industry sales based on Top 500 pharmaceutical and biotech companies.

Sales to 2016 based on company reported sales data. Sales for 2017 based on available company reported sales data. Sales forecasts to 2024 based on a consensus of leading equity analysts' estimates for company product sales and segmental sales.

All sales analysis based on EvaluatePharma®'s 'Orphan Drugs' sub-set of products, as defined in the Overview section.

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Top 100 USA Drug Cost per Patient per Year (2013-2017)

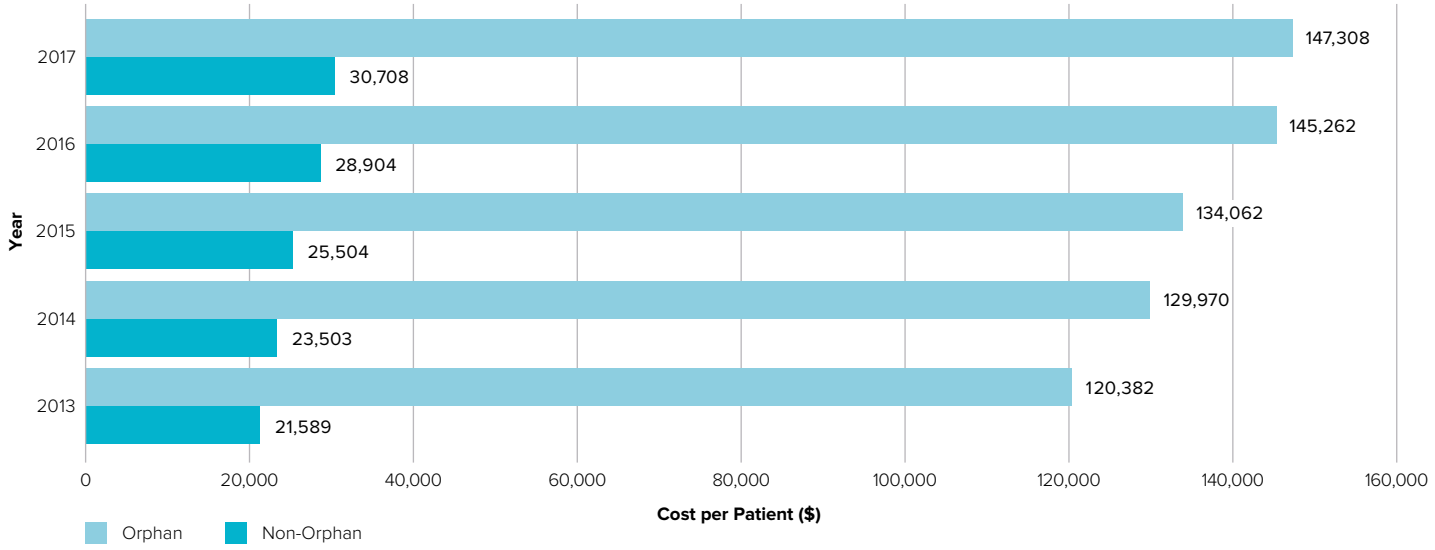
Mean orphan drug cost to USA patients $147,308 in 2017; median orphan drug cost $84,062.

EvaluatePharma® estimates that the mean cost per patient per year of an orphan drug was $147,308 versus $30,708 for a non-orphan drug (analysis based on the top 100 drugs in the USA in 2017). Whilst the drug price has increased year-on-year for both orphan and non-orphan drugs since 2013, the growth rate for both was significantly lower in 2017 compared to previous years which may be due to increasing pressure on drug developers to reduce to cost of treatment.

In 2017, seven drugs from our analysis had a mean cost of over $300,000 per patient. Of these seven, over half were drugs within the blood therapy category, highlighting the vital importance and demand for the development of successful therapies for rare blood disorders. Analysis showed increasing median prices for both orphan and non-orphan drugs, with the non-orphan drug prices displaying steeper increases, thus closing the considerable gap between non-orphan and orphan drug prices.

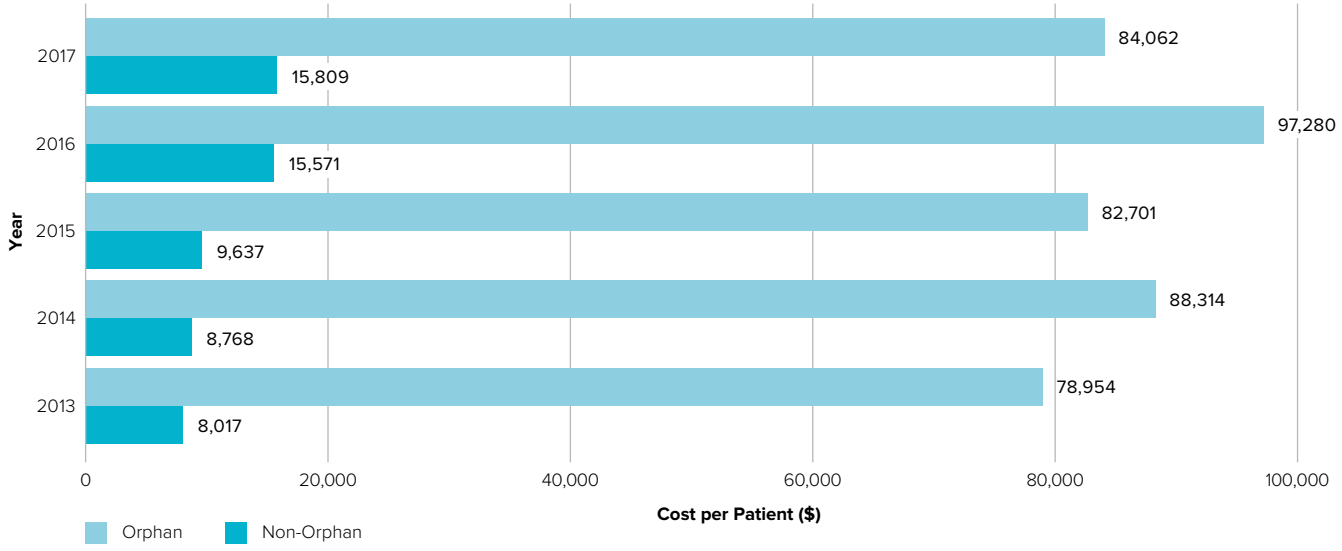
Mean Cost per Patient per Year (2013-2017)

Source: EvaluatePharma® May 2018



Median Cost per Patient per Year (2013-2017)

Source: EvaluatePharma® May 2018



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Top 100 Orphan and Non-Orphan USA Drugs by Sales Mean and Median Cost per Patient per Year (2013-2017)

Source: EvaluatePharma® May 2018

Cost per patient ($) per year		2013	2014	2015	2016	2017	CAGR
Orphan	Mean cost	120,382	129,970	134,062	145,262	147,308	5.2%
	Growth per year		8.0%	3.1%	8.4%	1.4%	
	Median cost	78,954	88,314	82,701	97,280	84,062	
Non-Orphan	Mean cost	21,589	23,503	25,504	28,904	30,708	9.2%
	Growth per year		8.9%	8.5%	13.3%	6.2%	
	Median cost	8,017	8,768	9,637	15,571	15,809	
Median cost differential (orphan/non-orphan)		9.8	10.1	8.6	6.2	5.3	
					Median price increase 2013/17:		
					Orphan:	1.06	
					Non-Orphan:	1.97	

Note: All sales analysis based on EvaluatePharma®'s 'Orphan Drugs' sub-set of products, as defined in the Overview section.

Cost per patient is an estimate for the retail cost of a drug to a patient, for a given year, based on a 100% compliance to the treatment guidelines outlined in the FDA label. Depending on the underlying pricing source data used, the price may or may not include off-invoice discounts. The Top 100 orphan and non orphan drugs were ranked by USA sales for 2017.

Prices for products in the US are sourced from Medicare Part B, NADAC, FSS and Medicaid. Availability of a price point determines choice of source. The source is kept consistent across years to reflect a clear trend in pricing.

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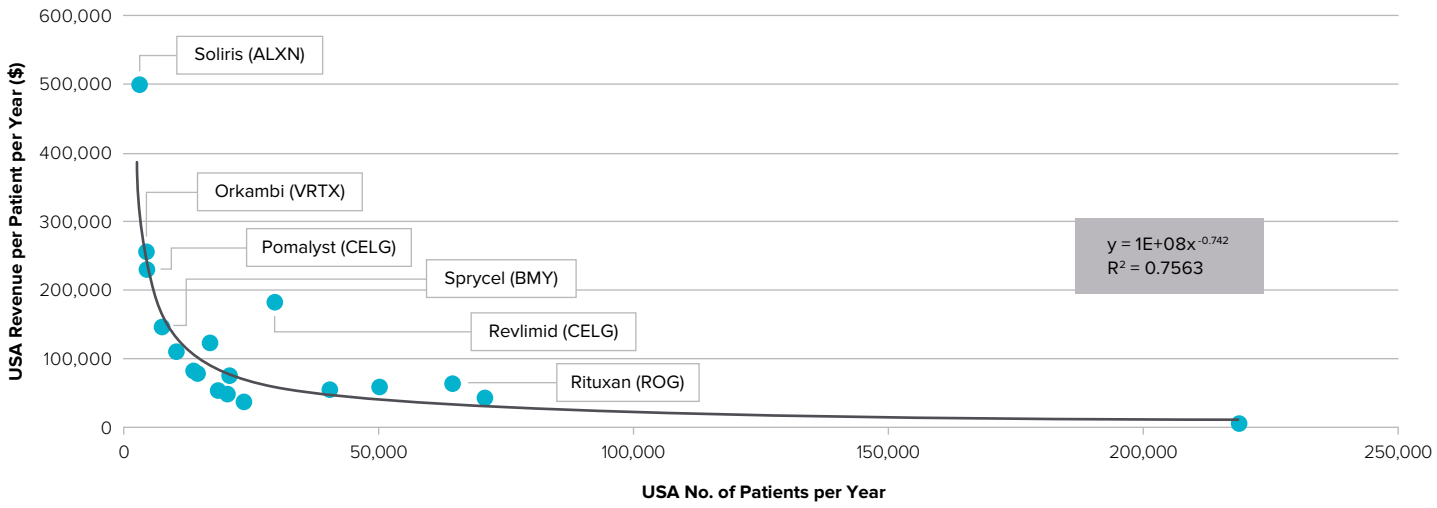
2017: USA Revenue per Patient per Year for Top 20 Selling Orphan Drugs

Soliris was the highest revenue generating orphan drug in 2017; revenue per patient and number of patients treated correlates with ultra-rare drugs achieving highest revenues per patient.

EvaluatePharma® discovered that, in general, as the number of patients treated increased, the revenue per patient decreased (based on the Top 20 selling orphan drugs in the USA). The strength of this correlation increased further for orphan drugs that treated fewer than 10,000 patients, confirming that there is the potential for big gains in those companies willing to invest in ultra-rare diseases. Soliris (eculizumab), originally developed to treat the rare blood disorder (paroxysmal nocturnal haemoglobinuria) continues to be the orphan drug that commands the highest revenue per patient in the USA, despite treating less than 2,500 patients in 2017.

Top 20 USA Orphan Drugs in 2017 by Sales; Revenue per Patient Vs. No. of Patients Treated

Source: EvaluatePharma® May 2018



USA Top 10 Selling Orphan Drugs in 2017 by Sales

Source: EvaluatePharma® May 2018

Rank	Product	Generic name	Company	USA sales ($m) 2017	Revenues per patient 2017*	No. of patients 2017
1.	**Revlimid**	lenalidomide	Celgene	5,426	184,011	29,487
2.	**Rituxan**	rituximab	Roche	4,199	65,009	64,594
3.	**Copaxone**	glatiramer acetate	Teva Pharmaceutical Industries	3,116	60,906	50,061
4.	**Opdivo**	nivolumab	Bristol-Myers Squibb	3,102	43,847	70,746
5.	**Keytruda**	pembrolizumab	Merck & Co	2,309	56,910	40,573
6.	**Imbruvica**	ibrutinib	AbbVie	2,144	126,820	16,906
7.	**Avonex**	interferon beta-1a	Biogen	1,594	78,262	20,367
8.	**Sensipar**	cinacalcet hydrochloride	Amgen	1,374	6,287	218,559
9.	**Soliris**	eculizumab	Alexion Pharmaceuticals	1,235	501,719	2,462
10.	**Xyrem**	sodium oxybate	Jazz Pharmaceuticals	1,187	81,624	14,539

*Revenues per patient: An estimate of the dollar ($) revenues per year received, by a company, per patient for a drug in the USA market. This takes into account the cost per patient (average mg per year multiplied by the cost per mg), off-invoice discount and patient compliance.

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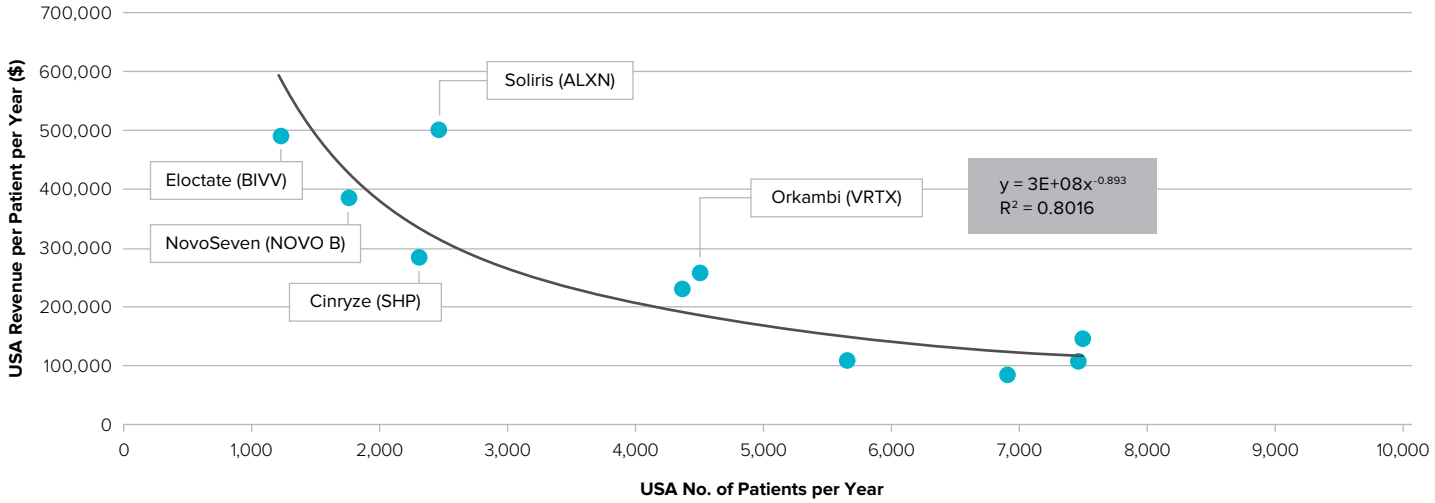
2017: USA Revenue per Patient per Year for Top 20 Selling Orphan Drugs

Top 10 USA Orphan Drugs in 2017 by Sales (fewer than 10,000 patients treated); Revenue per Patient Vs. No. of Patients Treated

Source: EvaluatePharma® May 2018



Note: Sales represent company reported sales where available, otherwise based on an average of equity analyst estimates.

USA sales represent sales for all indications.

EvaluatePharma® analysed the Top 10 selling USA drugs which treated fewer than 10,000 patients in 2017.

All sales analysis based on EvaluatePharma®'s 'Orphan Drugs' sub-set of products, as defined in the Overview section.

Prices for products in the US are sourced from Medicare Part B, NADAC, FSS and Medicaid. Availability of a price point determines choice of source. The source is kept consistent across years to reflect a clear trend in pricing.

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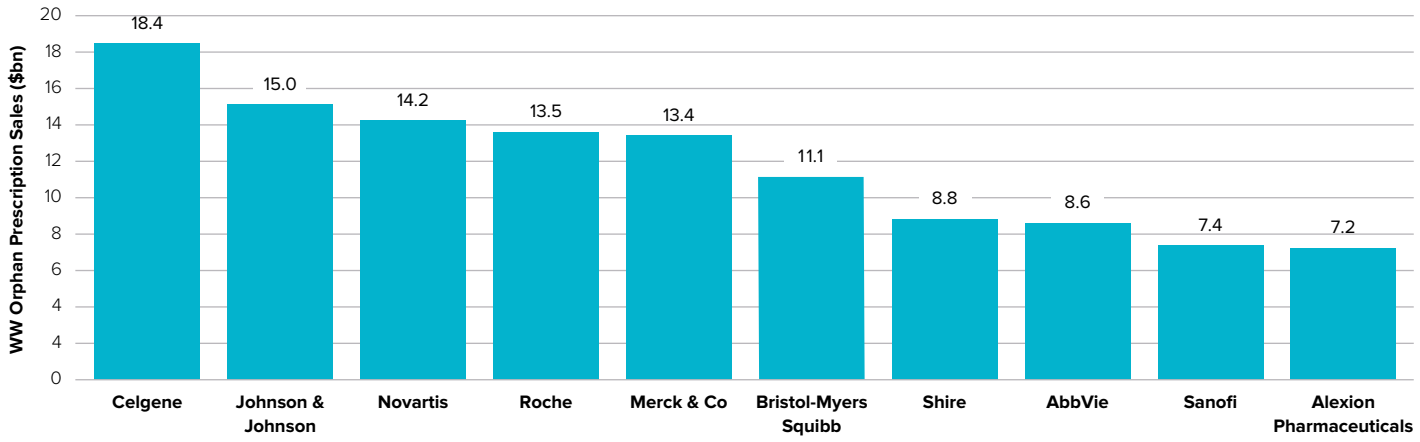
Worldwide Orphan Drug Sales in 2024: Top 20 Companies

Celgene is expected to be the leading company in the orphan drug market in 2024 with sales of $18.4bn; all other companies ranked in the top five are expected to achieve sales ranging from $13.4bn to $15bn.

EvaluatePharma® finds that anticipated strong sales of Revlimid Pomalyst (pomalidomide), Imbruvica (ibrutinib) and Darzalex (daratumumab) – all used to treat haematological malignancies – will result to Celgene and Johnson & Johnson being lead companies, by sales, of the worldwide orphan drug market in 2024. In fact, more than 60% of orphan drug sales assigned to the top 10 companies in 2024 are expected to come from sales in the oncology therapy area. Alexion Pharmaceuticals is the only company in the top 10 list that we do not anticipate to have any sales in oncology orphan indications in 2024. The main source of revenue for Alexion Pharmaceuticals is Soliris, which is used in the blood therapy area. Our analysis shows AstraZeneca will be ranked in 12th position in 2024, moving up 29 places from the company's current position. This change is due to expected strong uptake of Calquence (acalabrutinib) and increased sales of Lynparza (olaparib). Seven of the top 10 companies are major pharmaceutical companies and we expect these companies to account for 35% of the total 2024 orphan drug market.

Worldwide Orphan Prescription Drug Sales in 2024: Top 10 Companies

Source: EvaluatePharma® May 2018



Worldwide Orphan Drug Sales (2017-2024): Top 20 Companies & Total Market

Source: EvaluatePharma® May 2018

		WW orphan sales ($bn)			WW market share			Rank
Rank	Company	2017	2024	% CAGR 17-24	2017	2024	Chg. (+/-)	Chg. (+/-)
1.	**Celgene**	**10.0**	**18.4**	+9.0%	8.0%	7.0%	-1.0%	+2
2.	**Johnson & Johnson**	**5.0**	**15.0**	+17.1%	4.0%	5.7%	+1.8%	+5
3.	**Novartis**	**12.4**	**14.2**	+2.0%	9.9%	5.4%	-4.5%	-2
4.	**Roche**	**10.3**	**13.5**	+3.9%	8.2%	5.2%	-3.1%	-2
5.	**Merck & Co**	**5.3**	**13.4**	+14.2%	4.2%	5.1%	+0.9%	+1
6.	**Bristol-Myers Squibb**	**7.3**	**11.1**	+6.2%	5.8%	4.2%	-1.6%	-1
7.	**Shire**	**7.8**	**8.8**	+1.7%	6.2%	3.3%	-2.8%	-3
8.	**AbbVie**	**2.6**	**8.6**	+18.5%	2.1%	3.3%	+1.2%	+8
9.	**Sanofi**	**3.9**	**7.4**	+9.4%	3.1%	2.8%	-0.3%	+1
10.	**Alexion Pharmaceuticals**	**3.5**	**7.2**	+10.6%	2.8%	2.7%	-0.1%	+1
11.	**Pfizer**	**4.9**	**5.0**	+0.2%	3.9%	1.9%	-2.0%	-3
12.	**AstraZeneca**	**0.4**	**4.2**	+42.4%	0.3%	1.6%	+1.3%	+29
13.	**Amgen**	**3.3**	**3.8**	+2.2%	2.6%	1.5%	-1.2%	-
14.	**BioMarin Pharmaceutical**	**1.2**	**3.8**	+18.1%	0.9%	1.4%	+0.5%	+13

Top 15-20 continued over...

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Worldwide Orphan Drug Sales in 2024: Top 20 Companies

Rank	Company	WW orphan sales ($bn) 2017	2024	% CAGR 17-24	WW market share 2017	2024	Chg. (+/-)	Rank Chg. (+/-)
15.	**Vertex Pharmaceuticals**	**2.2**	**3.5**	+7.2%	1.7%	1.3%	-0.4%	+4
16.	**Biogen**	**3.0**	**3.4**	+1.7%	2.4%	1.3%	-1.1%	-1
17.	**Sorrento Therapeutics**	**-**	**3.3**	n/a	-	1.3%	-	-
18.	**Bayer**	**3.0**	**2.8**	-1.3%	2.4%	1.1%	-1.4%	-4
19.	**Incyte**	**1.2**	**2.7**	+12.3%	1.0%	1.0%	+0.1%	+6
20.	**Jazz Pharmaceuticals**	**1.6**	**2.6**	+7.5%	1.3%	1.0%	-0.3%	+3
	Total Top 20	**88.9**	**152.7**	+8.0%	71.0%	58.4%	-12.7%	
	Other	**36.3**	**108.9**	+17.0%	29.0%	41.6%		
	Total	**125**	**262**	+11.1%	100.0%	100.0%		

Note: All sales analysis based on EvaluatePharma®'s 'Orphan' sub-set of products, as defined in the Overview section. Total numbers reflect rounding.

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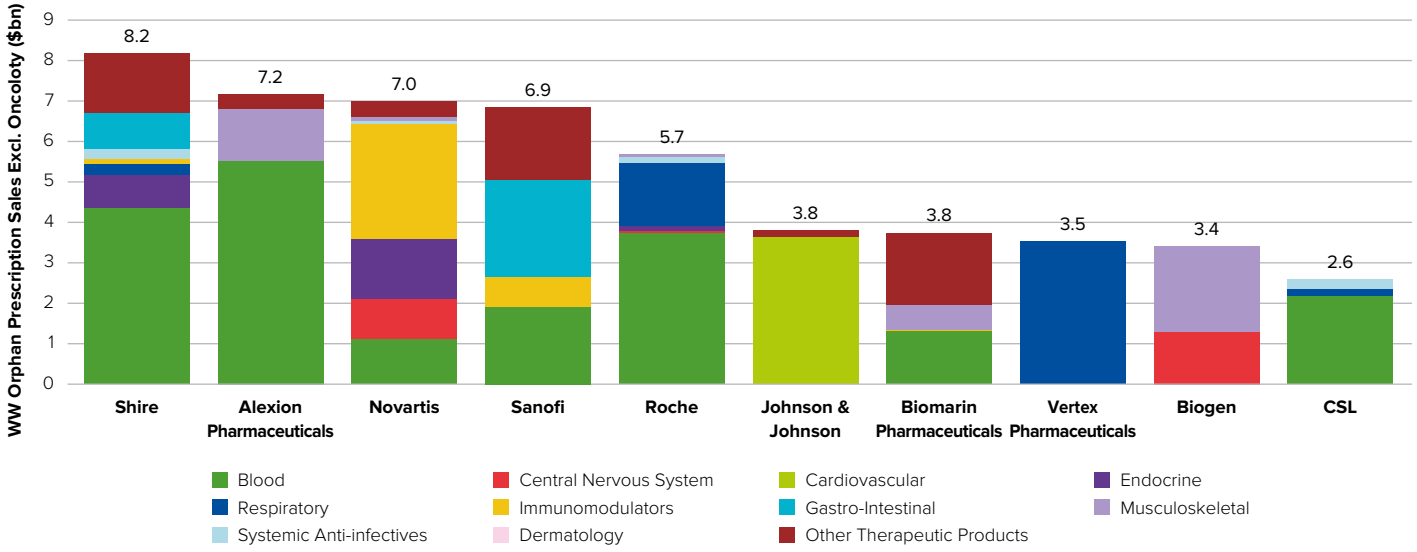
Worldwide Orphan Drug Sales in 2024 Excluding Oncology: Top 20 Companies

Shire and Alexion Pharmaceuticals lead EvaluatePharma's non-oncology company ranking in 2024, with both companies booking the majority of their sales in the blood therapy category.

EvaluatePharma® conducted a secondary analysis of the companies active in the orphan drug space excluding orphan products in the oncology therapy area. Despite an anticipated decrease in worldwide market share of 4.6% from 2017 to 2024, Shire is expected to remain the top selling company in this space and in 2024 to secure sales of $8.2bn, of which about half are forecast to come from blood indications. Only three companies in the top 10 – Johnson & Johnson, Vertex Pharmaceuticals and Biogen – are not expected to generate any revenue in 2024 from sales of orphan drugs in blood indications. Intercept Pharmaceuticals is expected be the 15th largest company in the non-oncology market space in 2024, moving up 37 positions from 2017, owing to a strong increase in sales of Ocaliva (obeticholic acid). The non-oncology space is expected to grow at a CAGR of 9.6% from 2017 to 2024, which is lower than the 12.7% CAGR expected in the oncology orphan drug market. Interestingly, sales of both non-oncology and oncology orphan drugs are each forecast to reach about $131bn in 2024. The top 20 companies in 2024 are forecast to represent about 56% of the non-oncology orphan market in 2024.

WW Orphan Drug Sales in 2024 by Therapy Category (Excluding Oncology): Top 10 Companies

Source: EvaluatePharma® May 2018



Worldwide Orphan Drug Sales Excluding Oncology: Top 20 Companies & Total Market

Source: EvaluatePharma® May 2018

		WW orphan sales ($bn)			WW market share			Rank
Rank	Company	2017	2024	% CAGR 17-24	2017	2024	Chg. (+/-)	Chg. (+/-)
1.	**Shire**	**7.5**	**8.2**	1%	10.9%	6.3%	-4.6%	-
2.	**Alexion Pharmaceuticals**	**3.5**	**7.2**	11%	5.2%	5.5%	0.3%	+2
3.	**Novartis**	**5.0**	**7.0**	6%	7.3%	5.3%	-2.0%	-1
4.	**Sanofi**	**3.5**	**6.9**	10%	5.2%	5.2%	0.1%	+1
5.	**Roche**	**2.0**	**5.7**	16%	3.0%	4.4%	+1.4%	+7
6.	**Johnson & Johnson**	**1.3**	**3.8**	16%	2.0%	2.9%	+1.0%	+12
7.	**BioMarin Pharmaceutical**	**1.2**	**3.8**	18%	1.7%	2.9%	+1.2%	+14
8.	**Vertex Pharmaceuticals**	**2.2**	**3.5**	7%	3.2%	2.7%	-0.5%	+3

Top 9-20 continued over...

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Worldwide Orphan Drug Sales in 2024 Excluding Oncology: Top 20 Companies

Rank	Company	WW orphan sales ($bn) 2016	2022	% CAGR 16-22	WW market share 2016	2022	Chg. (+/-)	Rank Chg. (+/-)
9.	**Biogen**	**3.0**	**3.4**	2%	4.4%	2.6%	-1.8%	-3
10.	**CSL**	**1.9**	**2.6**	5%	2.7%	2.0%	-0.7%	+4
11.	**Incyte**	**1.1**	**2.5**	12%	1.7%	1.9%	+0.3%	+11
12.	**Pfizer**	**2.4**	**2.4**	0%	3.5%	1.9%	-1.6%	-4
13.	**GW Pharmaceuticals**	**-**	**2.3**	n/a	-	1.8%	n/a	-
14.	**Novo Nordisk**	**2.6**	**2.1**	-3%	3.8%	1.6%	-2.2%	-7
15.	**Intercept Pharmaceuticals**	**0.1**	**1.9**	47%	0.2%	1.5%	+1.3%	+37
16.	**argenx**	**-**	**1.9**	n/a	-	1.5%	n/a	-
17.	**Athersys**	**-**	**1.9**	n/a	-	1.4%	n/a	-
18.	**Jazz Pharmaceuticals**	**1.3**	**1.8**	5%	2.0%	1.4%	-0.6%	-1
19.	**AveXis**	**-**	**1.8**	n/a	-	1.4%	n/a	-
20.	**bluebird bio**	**-**	**1.8**	n/a	-	1.4%	n/a	-
	Total Top 20	**39**	**73**	9%	56.6%	55.6%	-1.0%	
	Other	**29.8**	**58.1**	10%	43.4%	44.4%		
	Total	**69**	**131**	+9.6%	100.0%	100.0%		

Note: All sales analysis based on EvaluatePharma®'s 'Orphan' sub-set of products, as defined in the Overview section. Analysis excluded products categorised in the oncology therapeutic category to produce a non-oncology company list. Total numbers reflect rounding.

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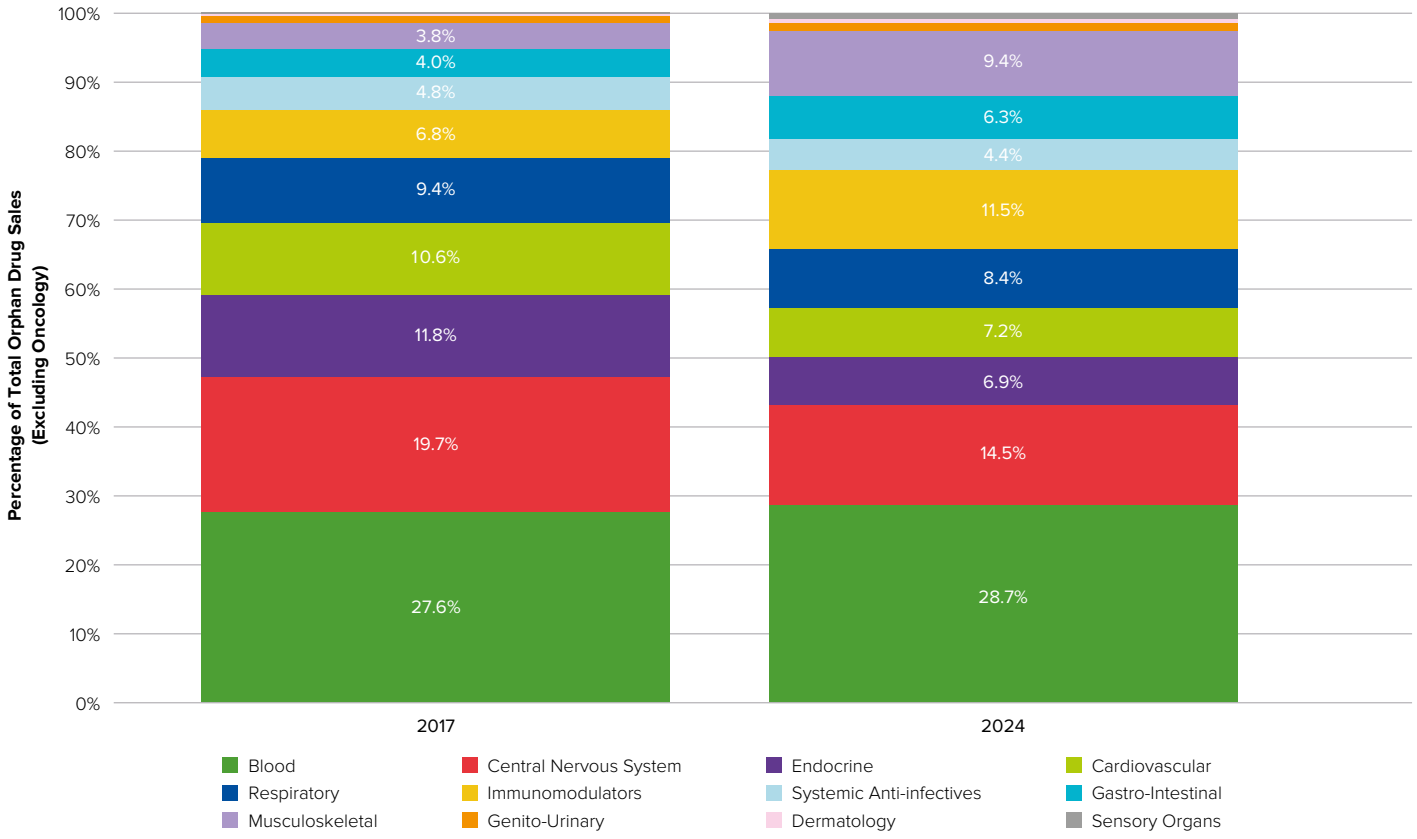
Share of Worldwide Orphan Drug Sales by Therapy Category (Excluding Oncology) and Lead Companies

Blood, and central nervous system are expected to be the leading therapy categories in the non-oncology space, together capturing about 43% of this market in 2024.

EvaluatePharma® finds that blood therapies command the largest share (around 28%) of the non-oncology worldwide orphan market, in both 2018 and 2024. Owing to high forecasted sales for Soliris, Alexion Pharmaceuticals is expected to remain the leading company in the blood therapy category. Driven by generic erosion of Copaxone (glatiramer acetate), the market share from products used in central nervous system indications will decrease from 19.7% in 2017 to 14.5% in 2024. This will also result in Teva Pharmaceuticals losing its position as lead company in this therapy category to GW Pharmaceuticals in 2024. The decrease in market share of endocrine therapies from 11.8% in 2017 to 6.9% in 2024 can be attributed to generic erosion of Amgen's Sensipar (cinacalcet). By 2024, Novartis will displace Amgen as leading company in this therapy category due to strong sales of Sandostatin LAR Depot (octreotide). The musculoskeletal therapy category will grow from 3.8% in 2017 to 9.4% in 2024 with Biogen remaining the sales leader in this category. The dermatology therapy category is expected to capture the lowest sales of all categories included in the non-oncology orphan drug market, with forecasted worldwide sales of $674m in 2024, equating to less than 1% of total market sales.

Share of Worldwide Orphan Drug Sales by Therapy Category (Excluding Oncology)

Source: EvaluatePharma® May 2018



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Worldwide Sales and Lead Company by Therapy Category (Excluding Oncology)

Source: EvaluatePharma® May 2018

	WW annual sales ($bn)		2017		2024	
Therapeutic category	2017	2024	Lead company	WW sales ($m)	Lead company	WW sales ($m)
Blood	17.3	33.8	**Shire**	4,721	**Alexion Pharmaceuticals**	5,503
Central Nervous System	12.3	17.1	**Teva Pharmaceutical Industries**	3,910	**GW Pharmaceuticals**	2,330
Endocrine	7.4	8.1	**Amgen**	1,730	**Novartis**	1,488
Cardiovascular	6.6	8.5	**United Therapeutics**	1,464	**Johnson & Johnson**	3,666
Respiratory	5.9	9.9	**Vertex Pharmaceuticals**	2,166	**Vertex Pharmaceuticals**	3,529
Immunomodulators	4.3	13.5	**Novartis**	1,296	**Novartis**	2,878
Systemic Anti-infectives	3.0	5.2	**Merck & Co**	787	**Emergent BioSolutions**	1,165
Gastro-Intestinal	2.5	7.5	**Sanofi**	1,707	**Sanofi**	2,398
Musculoskeletal	2.4	11.0	**Biogen**	884	**Biogen**	2,118
Genito-Urinary	0.7	1.3	**AMAG Pharmaceuticals**	387	**Retrophin**	457
Dermatology	0.19	0.7	**Torii Pharmaceutical**	125	**Fibrocell Science**	172
Sensory Organs	0.1	1.1	**Valeant Pharmaceuticals International**	37	**Spark Therapeutics**	930

Note: All sales analysis based on EvaluatePharma®'s 'Orphan' sub-set of products, as defined in the Overview section. Analysis excluded products categorised in the oncology therapeutic category to produce a non-oncology company list.

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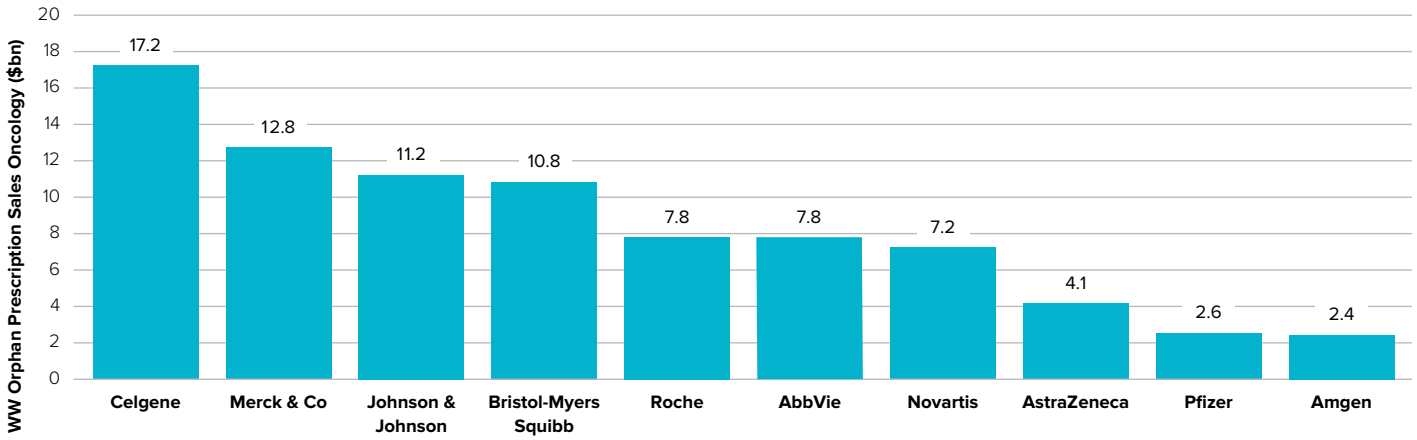
Worldwide Oncology Orphan Drug Sales in 2024: Top 20 Companies

All top 10 companies in the 2024 oncology orphan drug market are major pharmaceutical companies; Celgene is ranked in first position with sales of $17.2bn.

EvaluatePharma® finds that driven by sales of Revlimid, Celgene is expected to be the lead company in the oncology orphan drugs market in 2024. This is in-line with the forecast that Celgene will be the overall leading company in the orphan drug market in 2024, underscoring the high sales orphan oncology products command. The high sales expected from the programmed cell death (PD)-1 inhibitors, Keytruda and Opdivo (nivolumab), have resulted in Merck & Co and Bristol-Myers Squibb being respectively ranked in second and fourth position in 2024. Due to the expected increase in sales of Zejula (niraparib), TESARO will have the largest change in ranking and will move up 12 positions to 13th position in 2024. Bayer is expected to move down nine positions to 20th position, by 2024, owing to expected generic erosion of Nexavar (sorafenib). Overall, the top three companies in the oncology orphan drug market space – Celgene, Merck & Co and Johnson & Johnson – are expected to account for nearly a third of all sales in this segment in 2024.

Worldwide Oncology Orphan Drug Sales in 2024: Top 10 Companies

Source: EvaluatePharma® May 2018



Worldwide Oncology Orphan Drug Sales: Top 20 Companies & Total Market

Source: EvaluatePharma® May 2018

		WW orphan sales ($bn)			WW market share			Rank
Rank	Company	2017	2024	% CAGR 17-24	2017	2024	Chg. (+/-)	Chg. (+/-)
1.	**Celgene**	**10.0**	**17.2**	8%	17.7%	13.2%	-4.6%	-
2.	**Merck & Co**	**4.1**	**12.8**	18%	7.3%	9.8%	+2.5%	+3
3.	**Johnson & Johnson**	**3.6**	**11.2**	17%	6.4%	8.6%	+2.1%	+3
4.	**Bristol-Myers Squibb**	**7.2**	**10.8**	6%	12.7%	8.3%	-4.4%	-
5.	**Roche**	**8.3**	**7.8**	-1%	14.6%	6.0%	-8.6%	-3
6.	**AbbVie**	**2.3**	**7.8**	19%	4.0%	6.0%	+2.0%	+3
7.	**Novartis**	**7.4**	**7.2**	-2%	13.0%	5.5%	-7.5%	-4
8.	**AstraZeneca**	**0.3**	**4.1**	46%	0.5%	3.2%	+2.6%	+9
9.	**Pfizer**	**2.5**	**2.6**	0%	4.5%	2.0%	-2.5%	-1
10.	**Amgen**	**0.9**	**2.4**	15%	1.6%	1.9%	+0.3%	+2
11.	**Eisai**	**0.4**	**2.4**	29%	0.7%	1.9%	+1.1%	+3
12.	**Eli Lilly**	**3.1**	**2.3**	-5%	5.6%	1.7%	-3.8%	-5
13.	**TESARO**	**0.1**	**2.0**	52%	0.2%	1.5%	+1.4%	+12
14.	**Seattle Genetics**	**0.3**	**1.7**	27%	0.5%	1.3%	+0.7%	+2
15.	**Ono Pharmaceutical**	**0.8**	**1.6**	10%	1.5%	1.2%	-0.2%	-2

Top 16-20 continued over...

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Worldwide Oncology Orphan Drug Sales in 2024: Top 20 Companies

Rank	Company	WW orphan sales ($bn) 2017	2024	% CAGR 17-24	WW market share 2017	2024	Chg. (+/-)	Rank Chg. (+/-)
16.	**Kura Oncology**	**-**	**1.5**	n/a	-	1.2%	n/a	-
17.	**Gilead Sciences**	**0.2**	**1.5**	38%	0.3%	1.1%	+0.9%	+5
18.	**Epizyme**	**-**	**1.4**	n/a	-	1.1%	n/a	-
19.	**Array BioPharma**	**-**	**1.4**	n/a	-	1.0%	n/a	-
20.	**Bayer**	**1.0**	**1.3**	4%	1.8%	1.0%	-0.8%	-9
	Total Top 20	**52.6**	**101.2**	10%	93.0%	77.3%	-15.6%	
	Other	**4.0**	**29.7**	33%	7.0%	22.7%		
	Total	**57**	**131**	+12.7%	100.0%	100.0%		

Note: All sales analysis based on EvaluatePharma®'s 'Orphan' sub-set of products, as defined in the Overview section. Analysis excluded products categorised in the oncology therapeutic category to produce a non-oncology company list. Total numbers reflect rounding.

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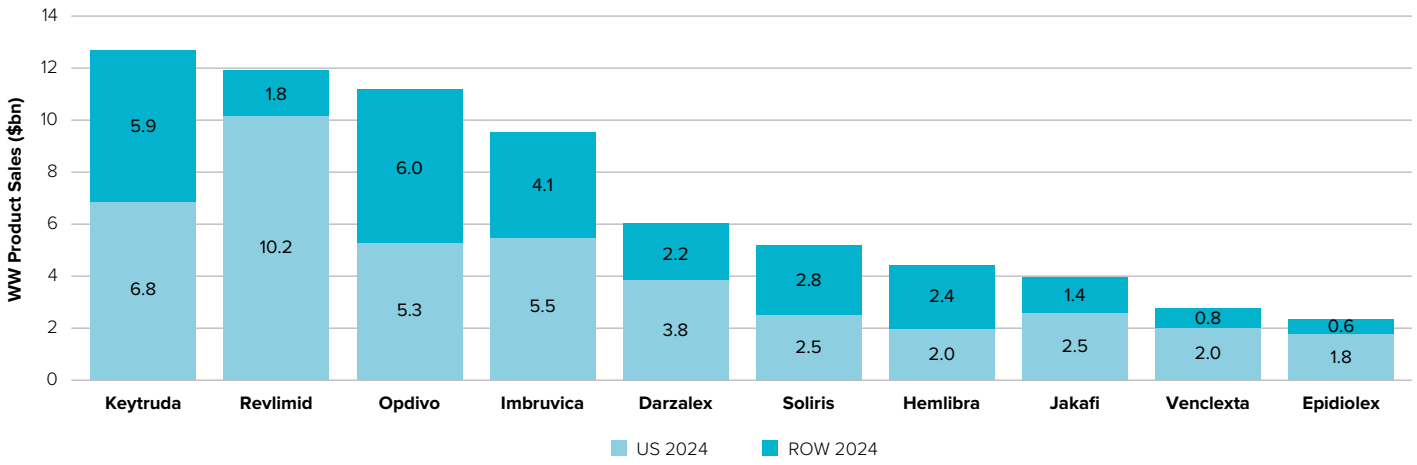
Worldwide Orphan Drug Sales: Top 20 Products

Keytruda is expected to be the leading orphan drug in 2024.

EvaluatePharma® finds that Keytruda (pembrolizumab) is the world's largest orphan drug in 2024, with total sales of $12.7bn and just over half these sales generated in the USA. Revlimid slides to second place with forecast sales of $11.9bn, 85% of which will stem from the USA. Other key movers include Hemlibra (emicizumab; +183% CAGR), Venclexta (venetoclax; +54% CAGR) and Zejula (+52% CAGR). Hemlibra launched in 2017 as a prophylactic for Haemophilia A, while Venclexta first launched in 2016, for the treatment of chronic lymphocytic leukaemia (CLL). Zejula launched in 2017, for the treatment of ovarian and fallopian tube cancer. Rituxan's (rituximab) sales are forecasted to decrease from $7.5bn in 2017 to $2.1bn (-17% CAGR) in 2024, owing to key patent expiry and consequent biosimilar adoption. Overall, the top 10 account for approximately 25% of the orphan drug market in 2024, with programmed cell death (PD)-1 inhibitors (Keytruda and Opdivio accounting for almost 10%.

Top 10 Selling Orphan Drugs in 2024 by Worldwide Sales (All Indications)

Source: EvaluatePharma® May 2018



Worldwide Top 20 Selling Orphan Drugs in 2024

Source: EvaluatePharma® May 2018

Rank	Product	Generic name	Company	Phase (current)	Mechanism of action	WW product sales ($bn) 2017	2024	CAGR
1.	**Keytruda**	pembrolizumab	Merck & Co/ Otsuka Holdings	Marketed	Programmed cell death protein 1 (PD1) antibody	3.8	**12.7**	+19%
2.	**Revlimid**	lenalidomide	Celgene/BeiGene	Marketed	Immunomodulator	8.2	**11.9**	+6%
3.	**Opdivo**	nivolumab	Bristol-Myers Squibb/Ono Pharmaceutical	Marketed	Programmed cell death protein 1 (PD1) antibody	5.7	**11.2**	+10%
4.	**Imbruvica**	ibrutinib	AbbVie/Johnson & Johnson	Marketed	Bruton's tyrosine kinase (BTK) inhibitor	3.2	**9.6**	+17%
5.	**Darzalex**	daratumumab	Johnson & Johnson	Marketed	Lymphocyte differentiation antigen CD38 antibody	1.2	**6.0**	+25%
6.	**Soliris**	eculizumab	Alexion Pharmaceuticals	Marketed	Complement factor C5 antibody	3.1	**5.2**	+7%
7.	**Hemlibra**	emicizumab	Roche/Chugai Pharmaceutical	Marketed	Coagulation factor IXa antibody; Coagulation factor X antibody	0.0	**4.4**	+183%
8.	**Jakafi**	ruxolitinib phosphate	Incyte/Novartis	Marketed	Janus kinase 1 (JAK1) inhibitor; Janus kinase 2 (JAK2) inhibitor	1.9	**3.9**	+11%
9.	**Venclexta**	venetoclax	AbbVie/Roche	Marketed	B-cell lymphoma 2 (BCL-2) inhibitor	0.1	**2.8**	+54%
10.	**Epidiolex**	cannabidiol	GW Pharmaceuticals	Filed	Cannabinoid (CB) receptor agonist	-	**2.3**	n/a

Top 11-20 continued over...

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Worldwide Orphan Drug Sales: Top 20 Products

Rank	Product	Generic name	Company	Phase (current)	Mechanism of action	WW product sales ($bn) 2017	2024	CAGR
11.	**Adcetris**	brentuximab vedotin	Seattle Genetics/ Takeda	Marketed	Tumour necrosis factor receptor superfamily member 8 (TNFRSF8) antibody	0.6	**2.2**	+20%
12.	**Lenvima**	lenvatinib mesylate	Eisai	Marketed	Vascular endothelial growth factor receptor (VEGFR) inhibitor	0.3	**2.2**	+34%
13.	**Pomalyst**	pomalidomide	Celgene	Marketed	Tumour necrosis factor alpha (TNFa) inhibitor	1.6	**2.2**	+4%
14.	**Lynparza**	olaparib	AstraZeneca	Marketed	Poly (ADP-ribose) polymerase 1 (PARP1) inhibitor; Poly (ADP-ribose) polymerase 3 (PARP3) inhibitor; Poly (ADP-ribose) polymerase (PARP) inhibitor	0.3	**2.2**	+33%
15.	**Rituxan**	rituximab	Roche	Marketed	B-lymphocyte antigen CD20 antibody	7.5	**2.1**	-17%
16.	**Spinraza**	nusinersen	Biogen	Marketed	Survival motor neuron 2 (SMN2) protein inhibitor	0.9	**2.1**	+13%
17.	**Gazyva**	obinutuzumab	Roche/Nippon Shinyaku	Marketed	B-lymphocyte antigen CD20 antibody	0.3	**2.1**	+33%
18.	**Zejula**	niraparib	TESARO	Marketed	Poly (ADP-ribose) polymerase 1 (PARP1) inhibitor; Poly (ADP-ribose) polymerase 2 (PARP2) inhibitor; Poly (ADP-ribose) polymerase (PARP) inhibitor	0.1	**2.0**	+52%
19.	**Uptravi**	selexipag	Johnson & Johnson/Nippon Shinyaku	Marketed	Prostacyclin receptor agonist	0.5	**2.0**	+21%
20.	**Ocaliva**	obeticholic acid	Intercept Pharmaceuticals/ Sumitomo Dainippon Pharma	Marketed	Bile acid receptor agonist	0.1	**2.0**	n/a
	Other					**85.5**	**170.3**	+12%
	Total					**125**	**262**	+13.1%

Note: Sales represent company reported sales where available, otherwise based on an average of equity analyst estimates.

Worldwide sales represent sales for all indications.

All sales analysis based on EvaluatePharma®'s 'Orphan' sub-set of products, as defined in the Overview section. Total numbers reflect rounding.

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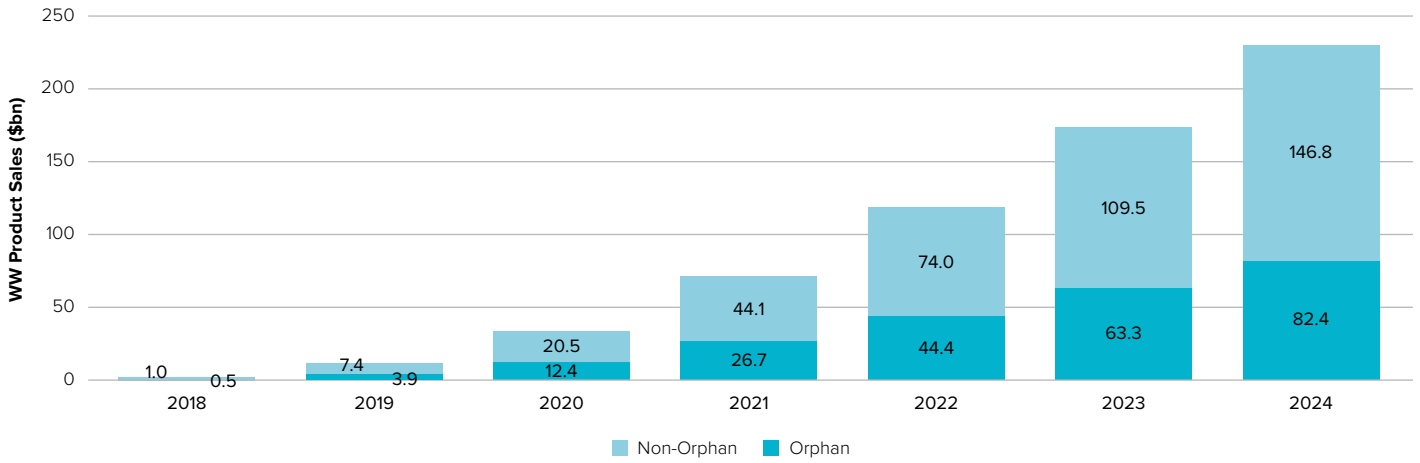
Worldwide Pipeline Sales to 2024: Orphan vs. Non-Orphan

Sales forecasts for pipeline orphan drugs account for over a third of total R&D pipeline sales through to 2024.

EvaluatePharma® finds that orphan products currently in R&D will account for 35-38% of sales generated from pipeline products from 2018 to 2024. The CAGR from 2018 to 2024 in the R&D orphan and non-orphan segments is comparable (133% for orphan products vs. 131% for non-orphan products. Hence, the value creation from orphan R&D products is not increasing more rapidly than from non-orphan R&D products. Both segments are likely to experience comparable healthy growth through to 2024. Oncology and blood indications dominate the orphan drug pipeline (see page 25) with the leading R&D blood product being Shire's lanadelumab with expected sales of nearly $1.6bn in 2024 and Array Biopharma's encorafenib in oncology, with forecasted sales of $825m in 2024. The top five R&D candidates account for 22% of the total NPV (Phase III to filed). By 2024, orphan drugs currently in R&D are expected to garner sales of over $82bn while non-orphan drugs in R&D are expected to generate sales of about $147bn.

Worldwide Pipeline Sales to 2024: Orphan vs. Non-Orphan

Source: EvaluatePharma® May 2018



Worldwide Pipeline: Orphan vs. Non-Orphan Drugs to 2024

Source: EvaluatePharma® May 2018

	WW sales ($bn)							
R&D pipeline	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**CAGR**
Orphan	0.5	3.9	12.4	26.7	44.4	63.3	82.4	+133%
Non-orphan	1.0	7.4	20.5	44.1	74.0	109.5	146.8	+131%
% Orphan sales	35%	35%	38%	38%	37%	37%	36%	
Total	**1.5**	**11.4**	**33.0**	**70.8**	**118.3**	**172.8**	**229.2**	**+132%**
Cumulative orphan	0.5	4.5	16.9	43.6	88.0	151.3	233.7	
Cumulative non-orphan	1.0	8.4	29.0	73.1	147.0	256.6	403.4	
Total							**637**	

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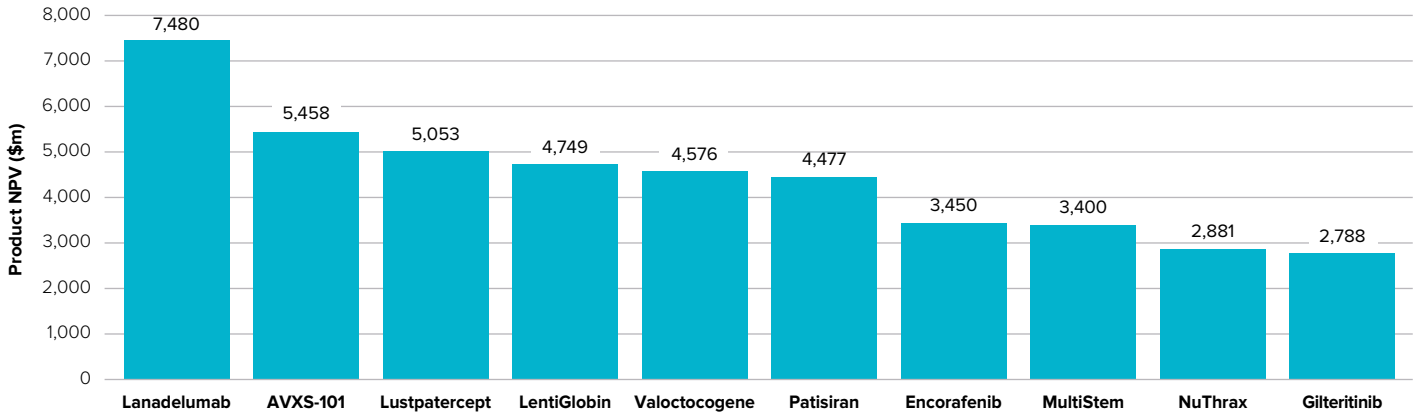
Top 20 Orphan R&D Products based on NPV

Of the top 20 orphan drugs currently in R&D, 40% could be blockbusters.

EvaluatePharma® finds that there are a number of potential blockbusters within the orphan drug pipeline. The top five orphan R&D drugs alone amass 20% of forecasted orphan drug pipeline sales in 2024. Lanadelumab (Shire) tops the list with an NPV of $7.5bn and is currently filed in the USA for the treatment of hereditary angioedema. Oncology and blood are the leading therapy areas, with the majority of the top 20 pipeline candidates being developed for indications in these areas. In addition, while 11 of the top 20 R&D candidates are being developed in-house, the remainder have been acquired or are in-licensed.

Top 10 Orphan Drugs in 2024 (Phase III/Filed) by NPV

Source: EvaluatePharma® May 2018



Worldwide Top 20 Orphan R&D Drugs Based on NPV (Sales, NPV)

Source: EvaluatePharma® May 2018

Rank	Product	Company	Phase (current)	Mechanism of action	Sales ($m) 2024	WW NPV ($m)	Strategy
1.	**Lanadelumab**	Shire	Filed	Kallikrein (KLK) antibody	1,569	**7,480**	Company acquisition
2.	**AVXS-101**	AveXis	Phase III	Survival of motor neuron (SMN) protein regulator	1,788	**5,458**	Organic
3.	**Luspatercept**	Celgene	Phase III	Activin receptor 2b antagonist	1,168	**5,053**	In-licensed
4.	**LentiGlobin**	bluebird bio	Phase III	Haemoglobin beta (HBB) gene therapy	1,615	**4,749**	Organic
5.	**Valoctocogene Roxaparvovec**	BioMarin Pharmaceutical	Phase III	Factor VIII gene regulator	1,318	**4,576**	In-licensed
6.	**Patisiran**	Alnylam Pharmaceuticals	Filed	Transthyretin (TTR) RNAi therapeutic	1,308	**4,477**	Organic
7.	**Encorafenib**	Array BioPharma	Filed	Serine/threonine-protein kinase B-Raf inhibitor	825	**3,450**	Product acquisition
8.	**MultiStem**	Athersys	Phase III	Tumour necrosis factor (TNF) cell therapy	1,852	**3,400**	Organic
9.	**NuThrax**	Emergent BioSolutions	Phase III	Bacillus anthracis immunoglobulin stimulant	1,102	**2,881**	Organic
10.	**Gilteritinib**	Astellas Pharma	Phase III	AXL inhibitor; FMS-like tyrosine kinase 3 (FLT3) inhibitor	905	**2,788**	In-licensed

Top 11-20 continued over...

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Top 20 Orphan R&D Products based on NPV

Rank	Product	Company	Phase (current)	Mechanism of action	Sales ($m) 2024	WW NPV ($m)	Strategy
11.	**Polatuzumab Vedotin**	Roche	Phase III	IgM membrane glycoprotein antibody	520	**2,632**	Organic
12.	**AndexXa**	Portola Pharmaceuticals	Filed	Coagulation factor Xa regulator	720	**2,316**	Organic
13.	**Selinexor**	Karyopharm Therapeutics	Phase III	Exportin (XPO)/chromosome region maintenance protein (CRM) 1 inhibitor	970	**2,315**	Company acquisition
14.	**Larotrectinib**	Loxo Oncology	Filed	Tropomyosin receptor kinase (Trk) inhibitor	694	**2,299**	In-licensed
15.	**ABL001**	Novartis	Phase III	Bcr/Abl fusion protein inhibitor	495	**2,286**	Organic
16.	**Rapastinel**	Allergan	Phase III	N-methyl-D-aspartate (NMDA) receptor regulator	676	**2,282**	Company acquisition
17.	**Ivosidenib**	Agios Pharmaceuticals	Filed	Isocitrate dehydrogenase 1 (IDH1) inhibitor	757	**2,119**	Organic
18.	**Fedratinib**	Celgene	Phase III	Janus kinase 2 (JAK2) inhibitor	460	**2,013**	Company acquisition
19.	**Vosoritide**	BioMarin Pharmaceutical	Phase III	Atrial natriuretic peptide receptor A (ANPRA) agonist; Fibroblast growth factor receptor 3 (FGFR3) inhibitor	627	**1,936**	Organic
20.	**Binimetinib**	Array BioPharma	Filed	Mitogen-activated protein kinase (MAPK) inhibitor	542	**1,931**	Organic
	Other				**22,045**	**59,078**	
	Total				**41,955**	**125,521**	
				vs. Non-Orphan:	**70,772**	**225,439**	

Note: Sales represent company reported sales where available, otherwise based on an average of equity analyst estimates.

Factor VIII products for haemophilia A & B classified as orphan drugs.

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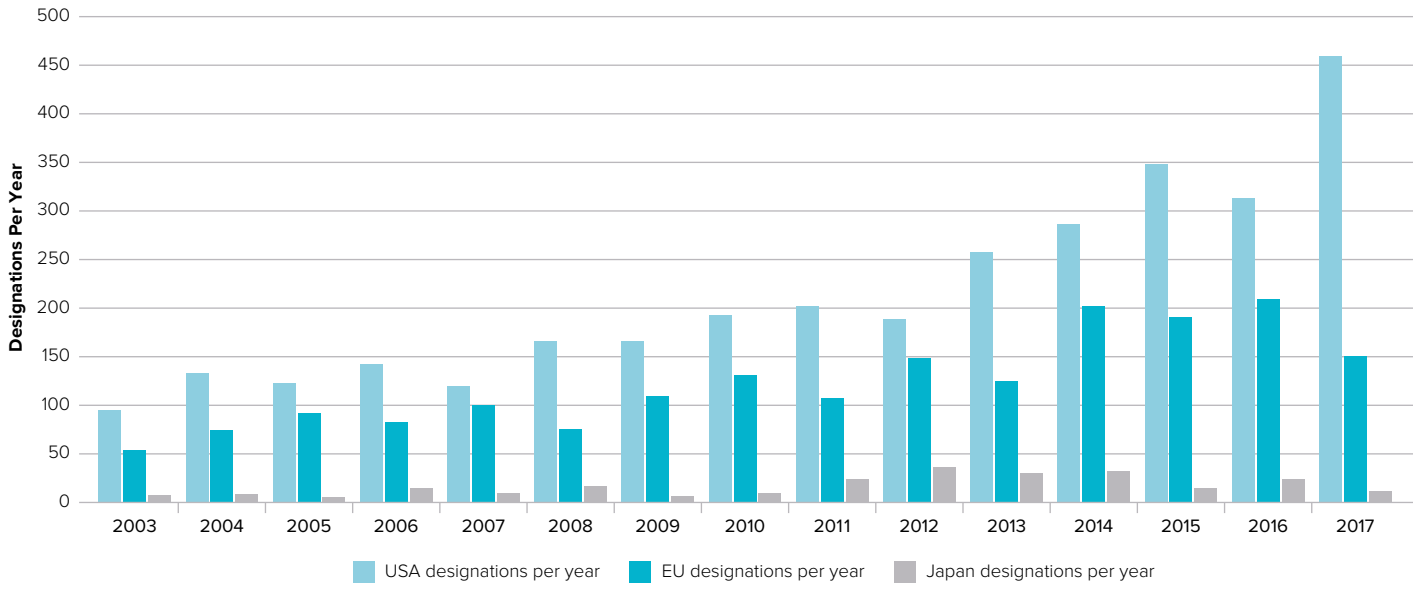
USA, EU & Japan Orphan Designations per Year (2003-2017)

The USA continues to lead the EU and Japan in granting orphan drug designations.

The number of orphan drug designations granted by the FDA in 2017 increased from 320 in 2016 to 459 in 2017. This 43% increase is likely due to a rise in number of requests for orphan drug designations and to the implementation of the orphan drug modernisation plan by the FDA, which aims to eliminate the agency's backlog of existing designation requests and to ensure timely review of new applications. Conversely, the number of orphan drug designation granted in 2017 in the EU and Japan was lower than in recent years. Furthermore, the cumulative number of orphan drug designations granted by the FDA is more than double the number granted by the EMA and nearly 10 times higher that granted by the MHLW.

USA, EU & Japan Orphan Designations per Year (2003-2017)

Source: EvaluatePharma® May 2018



USA, EU & Japan Orphan Designations per Year (2003-2017)

Source: EvaluatePharma® May 2018

	Orphan designations														
Year	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
USA designations per year	94	132	123	141	119	165	165	192	201	189	260	289	348	320	459
Growth per year		+40%	-7%	+15%	-16%	+39%	+0%	+16%	+5%	-6%	+38%	+11%	+20%	-8%	+43%
EU designations per year	54	74	91	82	100	74	109	130	107	148	124	201	191	210	150
Growth per year			+23%	-10%	+22%	-26%	+47%	+19%	-18%	+38%	-16%	+62%	-5%	+10%	-29%
Japan designations per year	7	8	5	14	10	16	7	10	24	36	30	32	14	23	11
Growth per year		+14%	-38%	+180%	-29%	+60%	-56%	+43%	+140%	+50%	-17%	+7%	-56%	+64%	-52%

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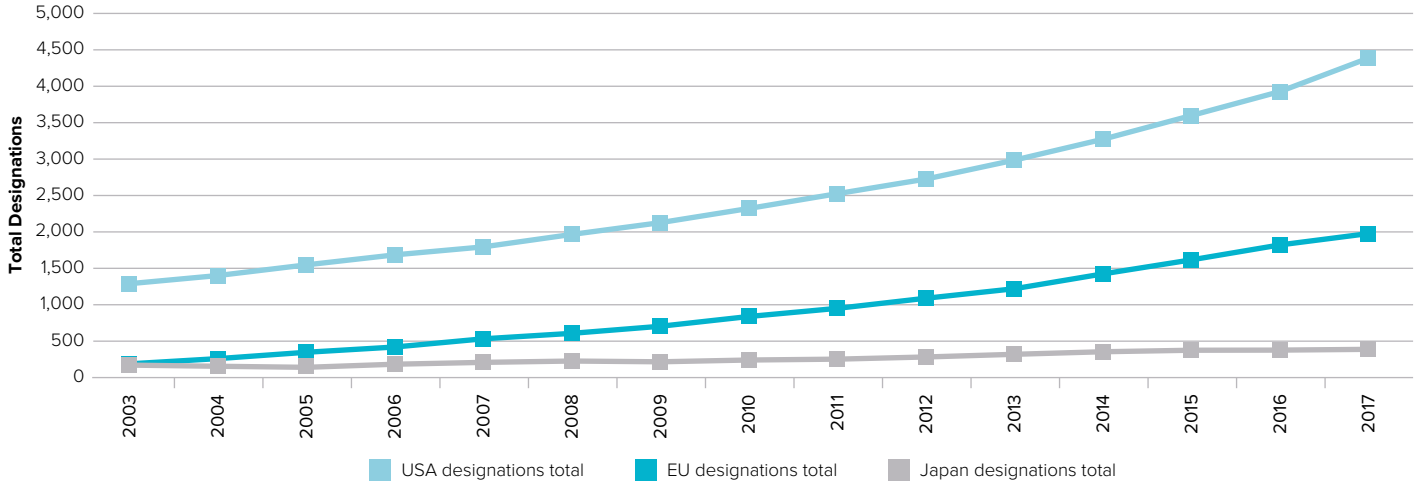
USA, EU & Japan Orphan Drug Designations Cumulative Total

Source: EvaluatePharma® May 2018



Cumulative US, EU & Japan Orphan Designations & US Approvals per Year (2003-2017)

Source: EvaluatePharma® May 2018

	Orphan designations cumulative total														
Year	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
USA designations total	1,283	1,415	1,538	1,679	1,798	1,963	2,128	2,320	2,521	2,709	2,967	3,254	3,601	3,914	4,373
Growth per year		+10%	+9%	+9%	+7%	+9%	+8%	+9%	+9%	+7%	+10%	+10%	+11%	+9%	+12%
EU designations total	182	256	347	429	529	603	712	842	949	1,097	1,221	1,422	1,613	1,823	1,973
Growth per year			+36%	+24%	+23%	+14%	+18%	+18%	+13%	+16%	+11%	+16%	+13%	+13%	+8%
Japan designations total	167	175	180	194	204	220	227	237	261	297	327	359	373	396	407
Growth per year		+5%	+3%	+8%	+5%	+8%	+3%	+4%	+10%	+14%	+10%	+10%	+4%	+6%	+3%

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EvaluatePharma's forward looking view of the market is hugely influential as it displays the consensus of expectations, which influence company stock market valuations. The forecasts of equity analysts reveal their perspectives on individual company performance, industry trends and the macro economic environment.

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To find out more about this report and Evaluate's range of services please contact us:

North America: Tom Moore
Tel: +1 617 573 9454 / Email: thomas.moore@evaluategroup.com

Rest of the World: Will Hau
Tel: +44 (0)20 7377 0800 / Email: will.hau@evaluategroup.com

Japan: Hiroshi Yamazaki
Tel: + 81 (0)80 1164 4754 / Email: hiroshi.yamazaki@evaluategroup.com

For general questions: Jennifer Dinkel
Tel: +1-617-936-7783 / Email: jennifer.dinkel@evaluategroup.com

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www.evaluate.com

Evaluate Headquarters
Evaluate Ltd.
11-29 Fashion Street
London E1 6PX
United Kingdom
T +44 (0)20 7377 0800
F +44 (0)20 7539 1801

Evaluate Americas
EvaluatePharma USA Inc.
60 State Street, Suite 1910
Boston, MA 02109
USA
T +1 617 573 9450
F +1 617 573 9542

Evaluate Asia Pacific
Evaluate Japan KK
Akasaka Garden City 4F
4-15-1 Akasaka, Minato-ku
Tokyo 107-0052
Japan
T +81 (0)80 1164 4754