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Orphan Medicines in Europe

Are they really breaking the bank?

February 2019

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The headlines we've all become accustomed to around orphan medicines

List prices are regularly quoted without managed access arrangements or note of confidential discounts


PharmaTimes online

NICE restricts NHS access to Alexion's £366K-a-year bone drug

8th February 2017

NICE National Institute for Health and Care Excellence


The Guardian view on new drugs: high hopes, higher prices

Editorial

The row over the cost of a cystic fibrosis treatment has prevented its use in the UK. These patients, many of them children, deserve better

'New drugs emerge not according to need, but when companies know they can make sizable profits from them.' Photograph: REB Images/Getty Images/Blend Images


BUSINESS HEADLINES

Sanders to pharma firm: Why are you charging $375,000 for life-saving drug?

MIAMI HERALD | Tuesday, Feb. 5, 2019, 7:00 p.m.

In a letter released Monday, Feb. 4, 2019, Sen. Bernie Sanders asked Catalyst Pharmaceuticals Inc. CEO Patrick McEnany why it is charging $375,000 for Firdapse, a drug that treats a rare autoimmune disease. (AP Photo/Alex Brandon)

US perspectives have recently increased their focus on high costs in light recent events, rather than budget impact


The Telegraph

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Drug costing £10 million per patient to become most expensive treatment on the NHS

The decision to approve Eculizumab comes after a decision to withdraw NHS funding for 25 treatments that would prolong the lives of cancer patients


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Why IS the NHS agreeing sky-high prices for life-saving drugs - then refusing to pay for them?

- Sherri Coleman, 41, spent a week paralysed, imprisoned in her upstairs bedroom
- Doctors said they couldn't give her the drugs she needed to enjoy a quality of life
- Sherri was born with a rare form of muscular dystrophy, inherited from her father
- In the past, such hard episodes were contained with the drug dichlorphenamide
- Until 2012 it was readily available on the NHS costing £400 for a year's supply
- The equivalent drug costs £35,000 for a year and the NHS say it is too expensive


Search | The Guardian | UK edition

Gene therapy for 'bubble baby' syndrome approved on NHS

GlaxoSmithKline's Strimvelis is the first such treatment to be funded in the UK

GlaxoSmithKline's Strimvelis gene therapy is said by Nice to improve patient survival. Photograph: Alamy Stock Photo

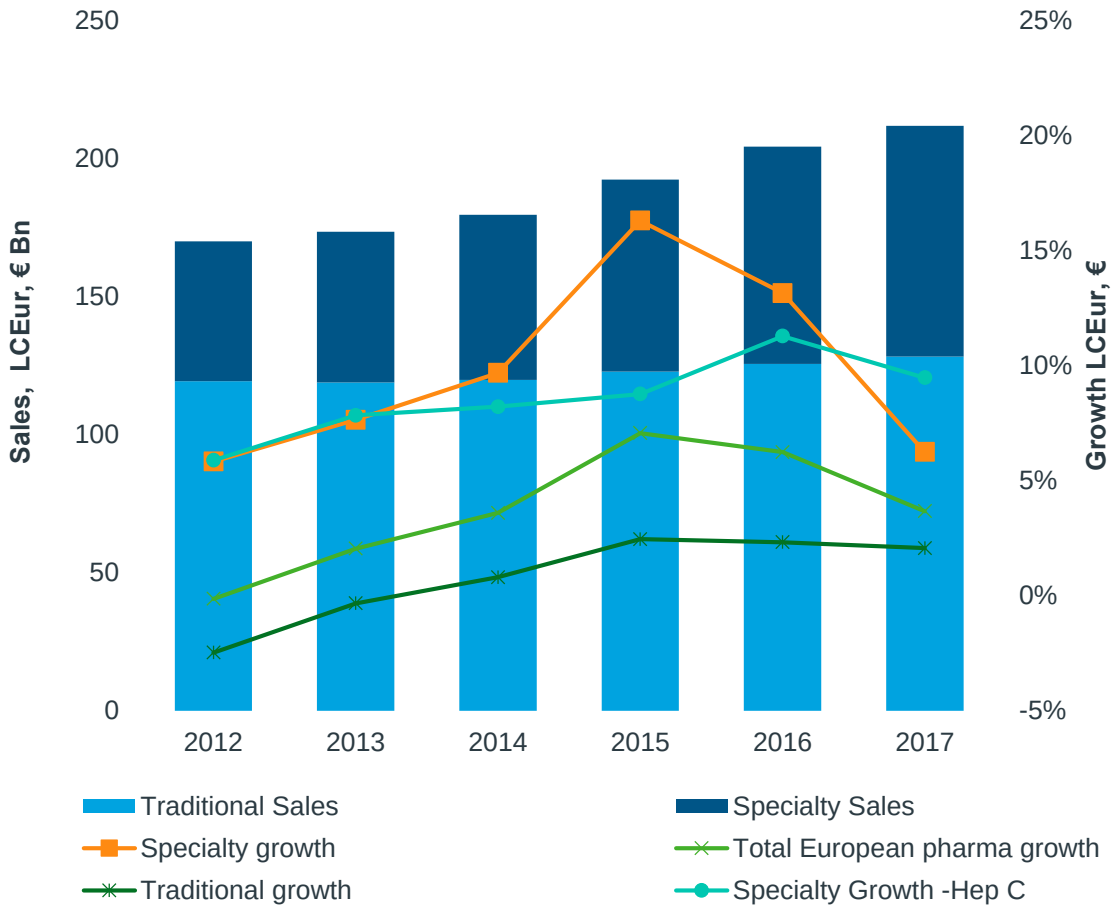
Orphan Medicines in Europe - Will They Really Break the Bank?

1. Uptake Trends for Orphan Medicines in Europe
2. Orphan Medicines in a Wider Budgetary and Uptake Context
3. Payer Moves to Collaborative Negotiations on Price

Spending on Specialty medicines has risen rapidly, growing faster than the total market

After the Hep C bubble, the European pharma growth rate dips to 4%

European specialty market trends, Sales and Growth

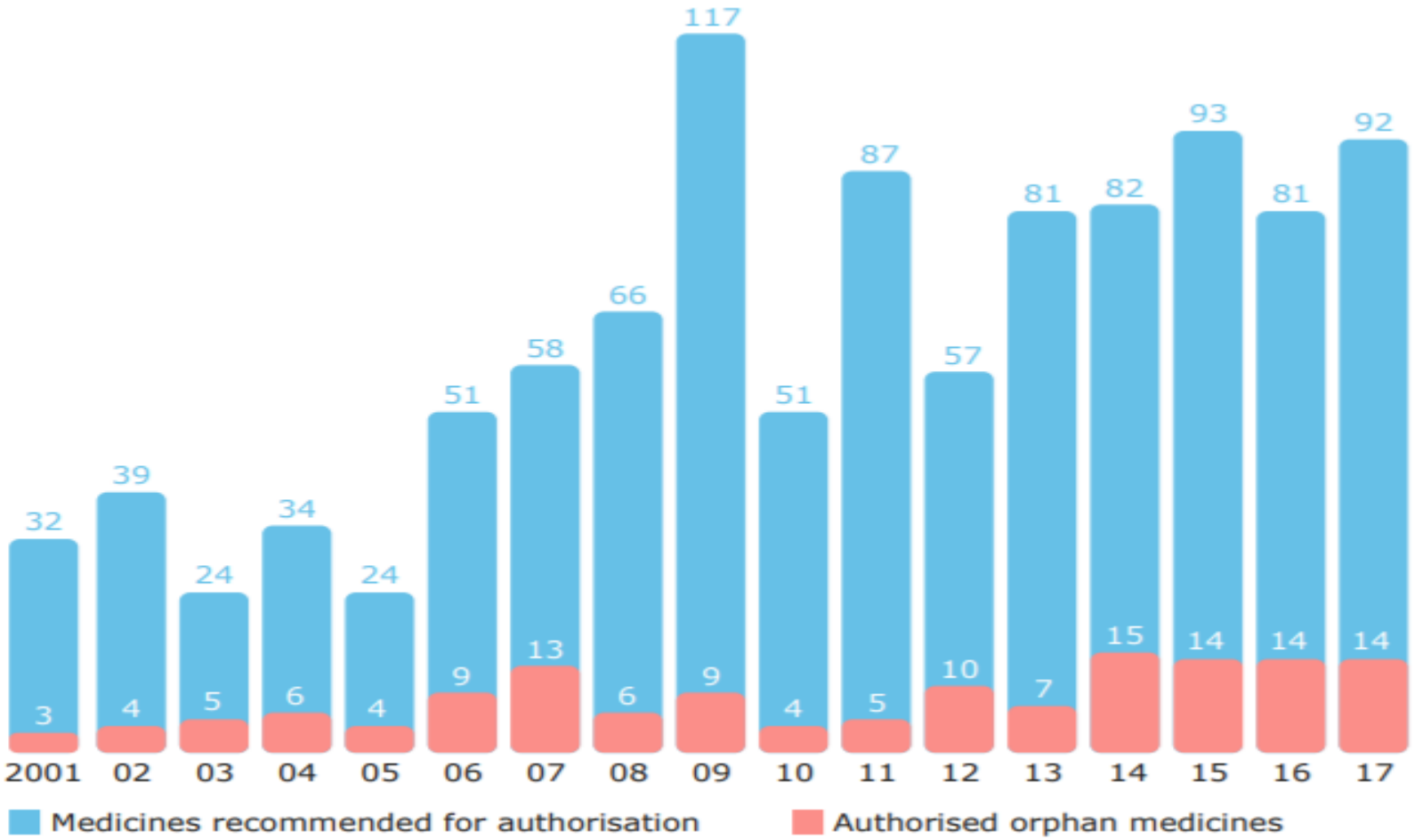


- After the ”HepC bubble”, the growth rate is down in low single digits in Europe
- Traditional medicine has very low value growth – but a sustained volume growth
- Specialty, consisting of several segments, shows a sustained growth

Source: IQVIA MIDAS MAT Q3 2017; Recent Hep C launches included: SOVALDI, HARVONI, VIEKIRAX, DAKLINZA, EPCLUSA, EXVIERA, PEGASYS, SOVRIAD, COPEGUS, ZEPATIER

Orphan medicines approvals in Europe haven risen substantially since 2000 legislation

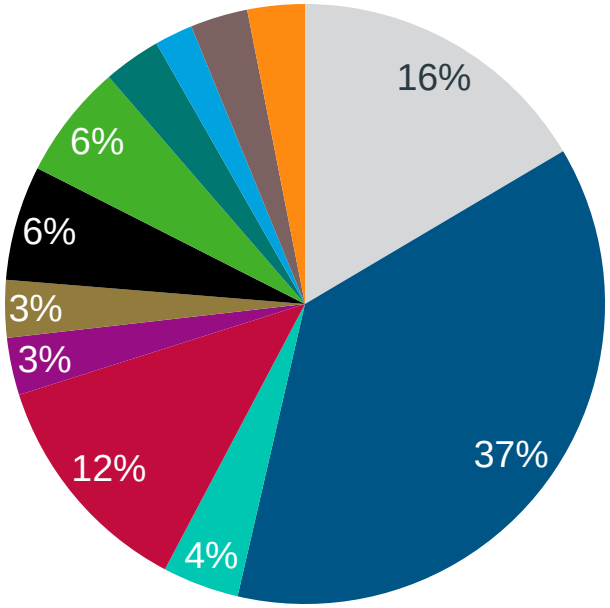
Number of total authorised medicines, and authorised orphan medicines



Source: EMA 2018

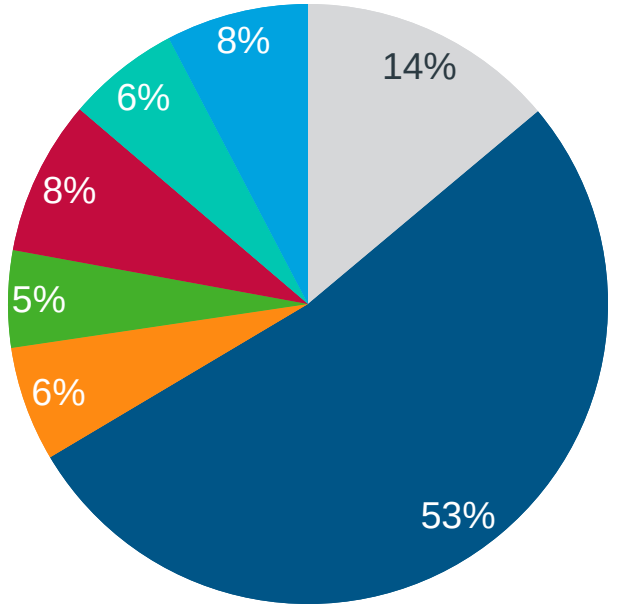
Oncology orphan medicines constitute 37% of all orphans and 53% of European Orphan medicines sales in 2018

Number of Orphan drugs



- Other
- Oncologics
- All Other Respiratory
- Other Alimentary Tract And Metabolism Products
- Antituberculars
- Hematopoietic Growth Factors
- GI medicines
- Other Cns
- Blood Coagulation
- Immunosupressants
- Cell and Gene Therapy
- Other Cardiovasculars

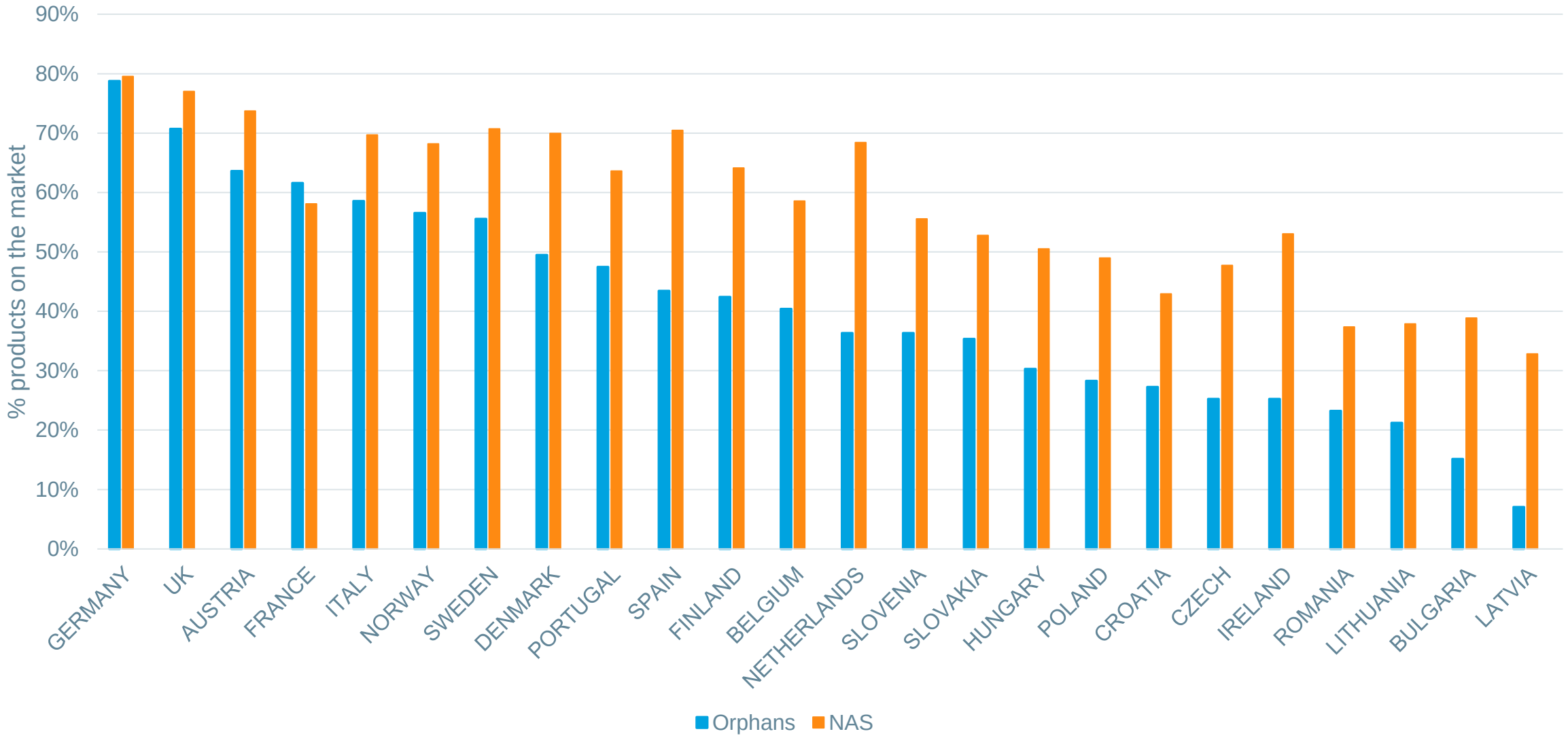
European Orphan drugs sales, 2018



Limitations: IQVIA MIDAS coverage may be subject to limitations where volumes are low or distributed through limited wholesaler or pharmacy networks and some product sales may be understated for lower volume products, which could include orphan drugs.

Source: IQVIA MIDAS MAT March 2018
Notes : All products included in number of product chart, only ones with sales data included in sales chart

Orphan availability vs New Active Substance (NAS) availability varies on a country level



Source: IQVIA European Thought Leadership

In 2016, 3.5% total pharma list price spend in Europe was on authorised Orphan drugs, ~ €6.4Bn

Country	Orphan Drug Sales 2016, €Mn	%MS of Orphan Drug sales 2016	Orphan Drugs Contribution to growth 2015-2016, LC€
GERMANY	1,717.6	**4.3%**	9.4%
FRANCE	1,077.0	3.6%	4.9%
ITALY	876.6	3.4%	2.6%
UK	857.4	**4.0%**	9.1%
SPAIN	617.0	3.2%	10.2%
BELGIUM	176.5	3.7%	**38.7%**
NETHERLANDS	155.6	3.2%	7.3%
SWEDEN	132.2	3.6%	9.0%
PORTUGAL	104.2	3.1%	-5.1%
AUSTRIA	103.3	2.8%	7.1%
DENMARK	86.3	3.7%	**16.8%**
IRELAND	63.8	3.2%	**14.6%**
NORWAY	62.4	3.6%	11.1%
POLAND	58.4	1.0%	-1.0%
HUNGARY	49.7	2.2%	7.5%
FINLAND	49.5	2.2%	6.8%
SLOVAKIA	41.4	3.0%	6.8%
CZECH REPUBLIC	37.5	2.0%	10.0%
ROMANIA	33.5	1.3%	0.1%
BULGARIA	26.4	2.2%	-7.0%
SLOVENIA	23.1	**4.1%**	**13.2%**
CROATIA	14.5	2.2%	1.0%
LITHUANIA	6.0	1.1%	-4.3%
ESTONIA*	4.1	1.8%	1.5%
LATVIA*	1.2	0.4%	-1.0%
GREECE*	0.6	0.0%	-6.3%
LUXEMBOURG*	0.4	0.2%	-11.4%
Total Europe	6,376.5	**3.5%**	**6.6%**

Key Observations:

- Of the €4.8Bn in spending increase in 2016 in Europe, Orphan drugs contributed 6.6% of growth.
- **Orphan drugs are a relatively small part of the drug budget in any country**
- **4 countries showing the highest orphan drug contribution to growth: Denmark, Belgium, Ireland and Slovenia**
- Countries where the Orphan Drugs sales is >= 4% of the total country sales in 2016: **Germany, Slovenia and UK**

Country	Orphan Drug Sales 2016, €Mn	%MS of Orphan Drug Sales 2016	Orphan Drugs Contribution to growth 2015-2016, LC€
Total Europe	6,376	**3.5%**	**6.6%**

Limitations: IQVIA MIDAS coverage may be subject to limitations where volumes are low or distributed through limited wholesaler or pharmacy networks and some product sales may be understated for lower volume products, which could include orphan drugs.

Source: IQVIA MIDAS MAT Dec 2016; *Estonia, Greece, Latvia & Luxembourg Retail Panels Only; Orphan drugs list from EMA Oct 2017 and Orphanet July 2016 downloads; Sales in Euros (absolute); Total Market includes Rx &non Rx

Despite the usually high unmet need in rare diseases, orphan drugs face challenges with pricing, reimbursement and access

Kalydeco experienced substantial access delays due to price – first sales 3 years after launch

kalydeco (ivacaftor) tablets

Vertex refuses £500m offer over 5 years from NICE for Cystic Fibrosis drug **Orkambi.** Current cost is £100k/year.

ORKAMBI (lumacaftor/ivacaftor) 200/125 mg • 100/125 mg tablets

Pfizer almost withdrew **Bosulif** from the market due to high AMNOG rebate

Bosulif bosutinib 500mg tablets

Recommendation to not reimburse **Translarna** for treatment of Duchenne Muscular Dystrophy

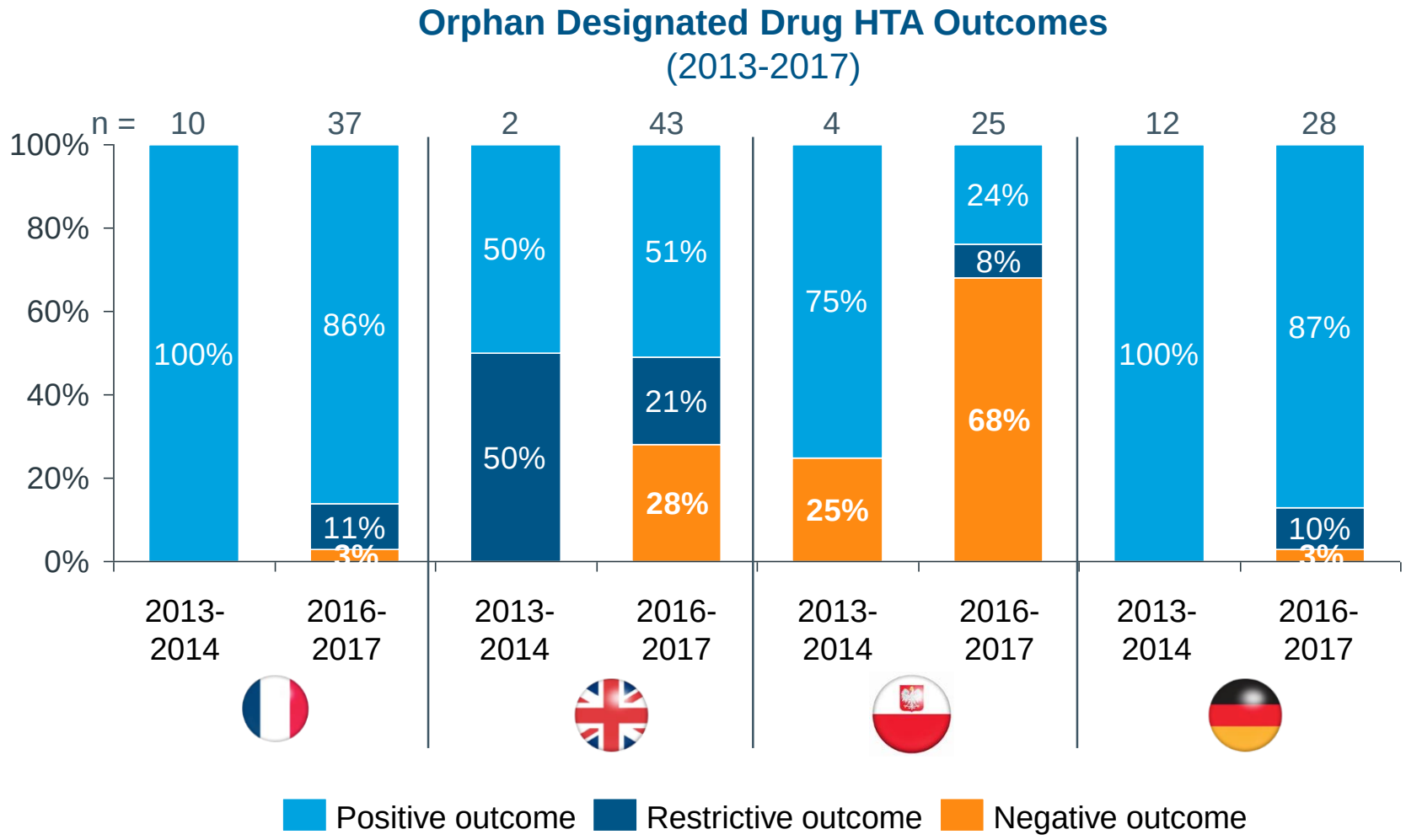
TRANSLARNA

Challenging price-related market access

US insurers are not convinced there is a demonstrated clinical benefit to **Exondys 51**, following only one trial of 12 patients and are pushing back on paying for the treatment

EXONDYS 51 (eteplirsen) Injection

Restricted or negative outcomes are becoming more common in Orphan Medicines assessments

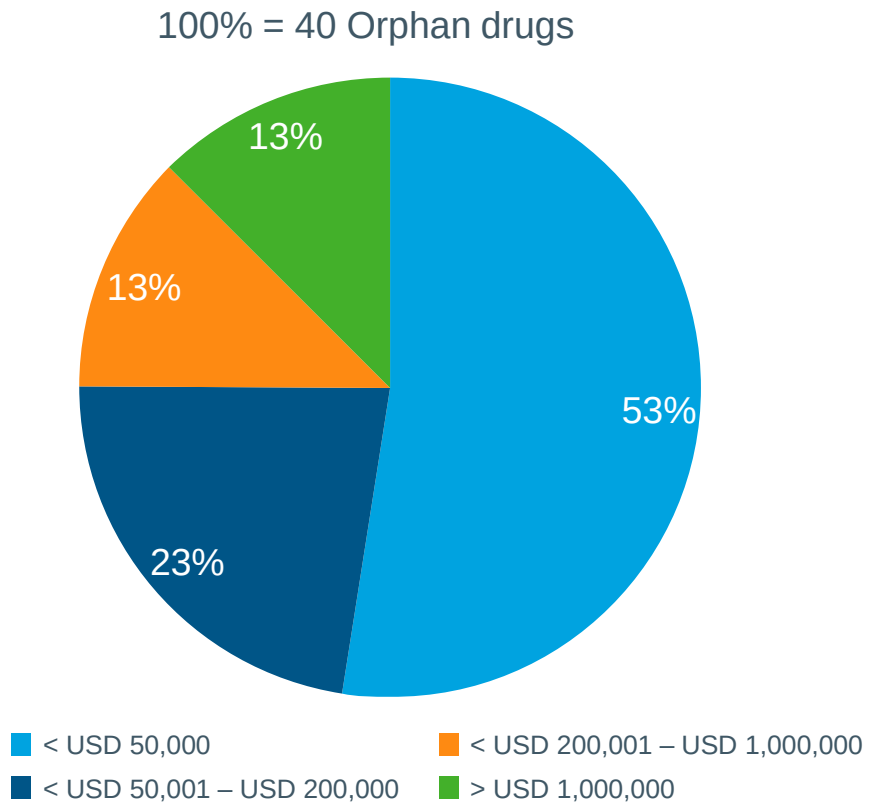


Source: IQVIA HTA Accelerator, Jan 2018

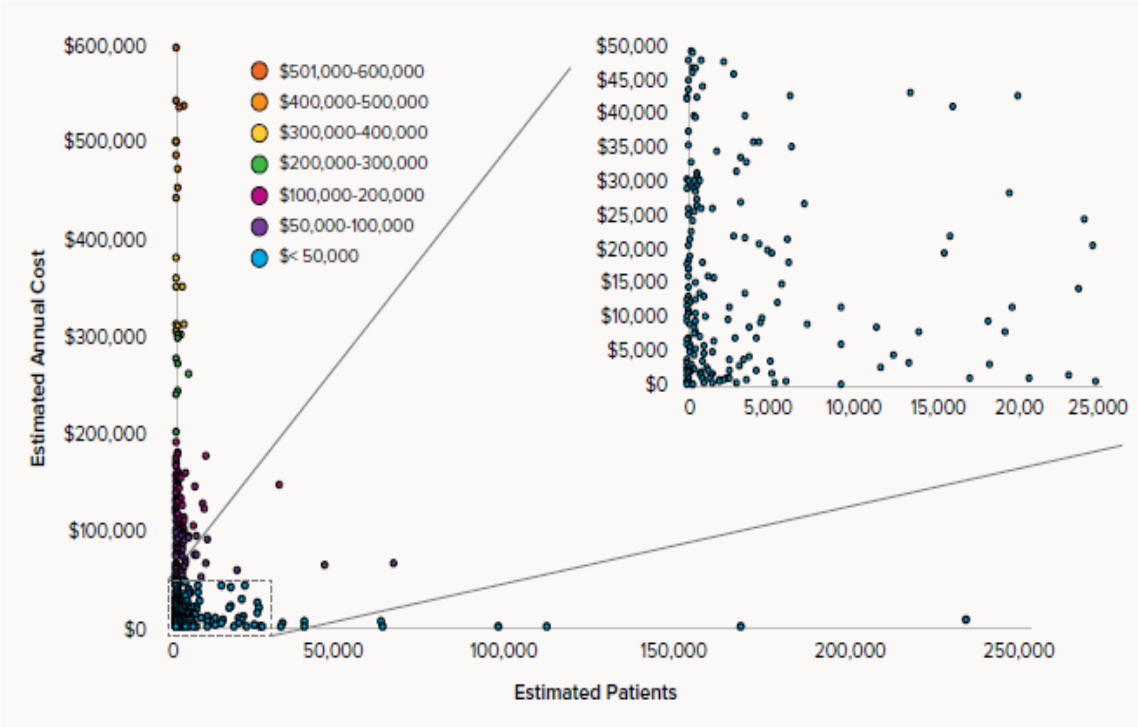
Positive = full access as per label; Restricted = access but with label restrictions; Negative = no access granted

The annual cost of the majority of orphan medicines in Europe is below $50,000, while the median annual cost per OD in the US is ~$32,000

Orphan Drug Distribution by Annual Cost (average list price by indication), EU 2017



Orphan Drug Distribution by Annual Cost, US, 2016



Price sources:
1. IQVIA Pricing Insights
2. IQVIA analysis

Payers developing collaborative measures to ‘get a grip’ on prices for rare disease medicines

Prioritisation of rare diseases will have to occur in order to manage budget impact

EU commission exploring EU wide pharmaceutical price control measures, centred around collaboration and price transparency

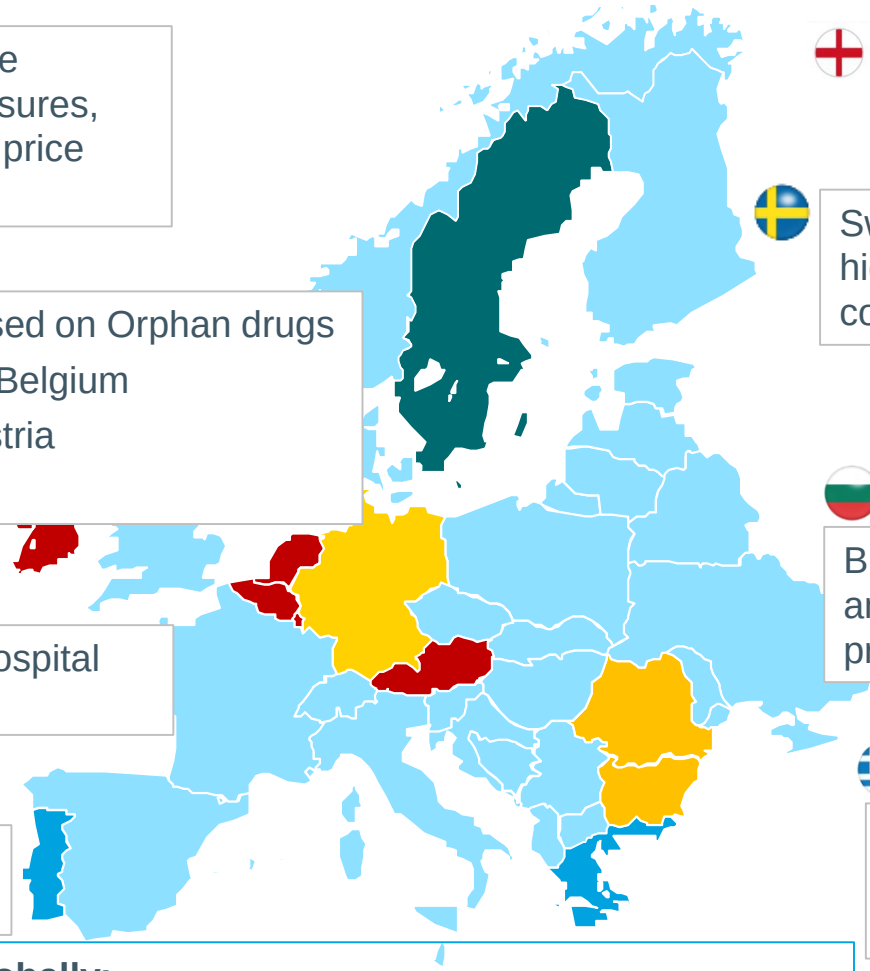
NHS England commercial effectiveness team negotiating after NICE rejection. Introduction of real world studies combined with price negotiation

Sweden increasing joint purchasing of high cost drugs across county councils

Joint purchasing agreement focused on Orphan drugs

- Pioneered by Netherlands and Belgium
- Joined by Luxembourg and Austria
- Ireland announced it would join

Possible reduction of threshold for automatic additional benefit in Germany



Bulgaria and Romania have entered an agreement to jointly negotiate pricing and availability

Dutch insurers introducing joint hospital purchasing schemes for biologics

Italy restricting confidential pricing agreements

Greece, Portugal, Spain and Italy have called for greater collaboration within the EU to drive down prices

Globally:

- Further establishment of **registries**
- Continued use of **Outcomes-based agreements**

Average NICE and SMC ICER of orphan and non-orphan drugs (drug with positive recommendations only)

- For recommended technologies the ICERs of orphans are almost 2 times higher for orphans than for non-orphans
- These data suggest that both organizations may be implicitly adjusting their willingness to pay for medicines that target rare diseases, although in the case of NICE the decisions made on oncology drugs (orphan and non-orphan) will also be influenced by application of the End-of-Life (EoL) guidance. In

	SMC	NICE
Orphan drugs	£46,211	£43,918
Non-orphan drugs	£24,090	£25,051

Sources: SMC https://www.scottishmedicines.org.uk/; NICE https://www.nice.org.uk/

The research proposes one general method for establishing a reasonable price for an orphan drug, based on the proposition that rates of return for investments in developing orphan drugs should not be greater than the industry average

Berdud, M., Drummond, M., & Towse, A. (2018). Establishing a Reasonable Price for an Orphan Drug. OHE Research Paper 18/05, London: Office of Health Economics. Available at: *https://www.ohe.org/.../**establishing-reasonable-price-orphan-drug***

There is a growing tendency towards increased need for real world evidence, and orphan drugs are not insulated from this

Key driver of change

Poor real-world drug performances and major safety issues
Recent failures of high profile products to demonstrate outcomes e.g. interferons for MS, ezetimibe for CVD, and major safety issues e.g. Actos and Avandia for diabetes, have led to increased clinical scrutiny from payers

Impact on pricing and market access

Increased at-launch data expectation
More critical assessment of efficacy, safety, tolerability and adverse event data at launch

Post-launch requirements for real world evidence
Move to re-evaluate products post-launch, when limited trial data is available at launch

- Payers increasingly insisting on RWE studies to justify costs and more importantly balance risk
- It can be difficult to demonstrate the value in the rare disease area as it is often not possible to do longitudinal natural history studies due to limited patient registry availability
- Added benefit that can't be quantified now, and will be defined later based on clinical experience
- Usually approved through conditional approval, still investing in clinical trials
- Predictive analytics should play an important role in identifying patients in the future

- pending local legal approval-

Novel Managed Access Agreement-underpinned by RWE study

Strensiq® (asfotase alfa) for injection

- Draft NICE recommendation (babies)
- **After negotiations**: expanded indication (infants, children and adult patients, and an updated draft NICE recommendation

- 5-year managed access agreement between NHSE and Alexion
- Goodwill and flexibility from pharma, and collaborative funding arrangements for rare disease treatments
- Value-based risk sharing agreement to provide wider cost-effective access for patients, informed by their first-hand experience of the ongoing impact that treatment is having on their health

- Strensiq has come about as a new 'managed access agreement
- It will broaden access of asfotase alfa to infants, children and adult patients with paediatric-onset HPP, who experience the most disabling symptoms and are expected to benefit most from therapy.
- It is a novel deal because it is a value-based risk sharing agreement to provide wider cost-effective access for patients, informed by their **first-hand experience of the ongoing impact that treatment is having on their health and quality of life**.
- The MA Agreement allows for a **five year period** to gather real-world data about how well the treatment benefits patients, before longer term commissioning decisions are taken.

In the UK, IQVIA & GeL announced 5 year partnership to enable Real-World clinical-genomics research and trials in Life Sciences

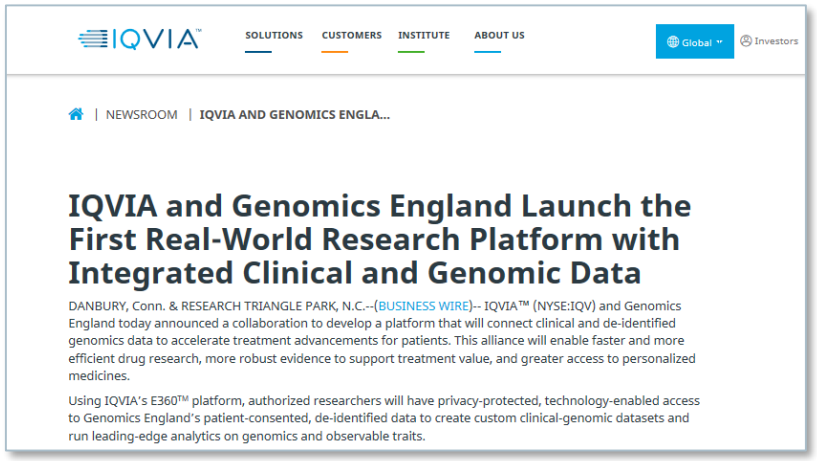
Genomics england

- Genomic data
  - ✓ Genomics expertise
  - ✓ Genomics data and specimen pipeline
- Technology
  - ✓ Genomics data management
  - ✓ Privacy & data governance
- Network
  - ✓ NHS knowledge and connections
  - ✓ Discovery forum
  - ✓ GeCIP
- Genomics development
  - ✓ Data interpretation

Genomic data is a critical element to transform clinical research and healthcare delivery

IQVIA

- Clinical data management
  - ✓ Clinical data models (eg,OMOP)
  - ✓ International data curation & standardization
- Technology
  - ✓ E360™
  - ✓ Privacy Analytics
- Industry engagement
  - ✓ Established customer base
- CRO, trials and network
- Healthcare analytics services to NHS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NEWSROOM | IQVIA AND GENOMICS ENGLA...

IQVIA and Genomics England Launch the First Real-World Research Platform with Integrated Clinical and Genomic Data

DANBURY, Conn. & RESEARCH TRIANGLE PARK, N.C.--(BUSINESS WIRE)-- IQVIA™ (NYSE:IQV) and Genomics England today announced a collaboration to develop a platform that will connect clinical and de-identified genomics data to accelerate treatment advancements for patients. This alliance will enable faster and more efficient drug research, more robust evidence to support treatment value, and greater access to personalized medicines.

Using IQVIA's E360™ platform, authorized researchers will have privacy-protected, technology-enabled access to Genomics England's patient-consented, de-identified data to create custom clinical-genomic datasets and run leading-edge analytics on genomics and observable traits.

UK genomics vision announced October 2, 2018

Genomics england

Matt Hancock the Secretary of State for Health and Social Care, announced an ambitious vision for genomic healthcare in the UK…

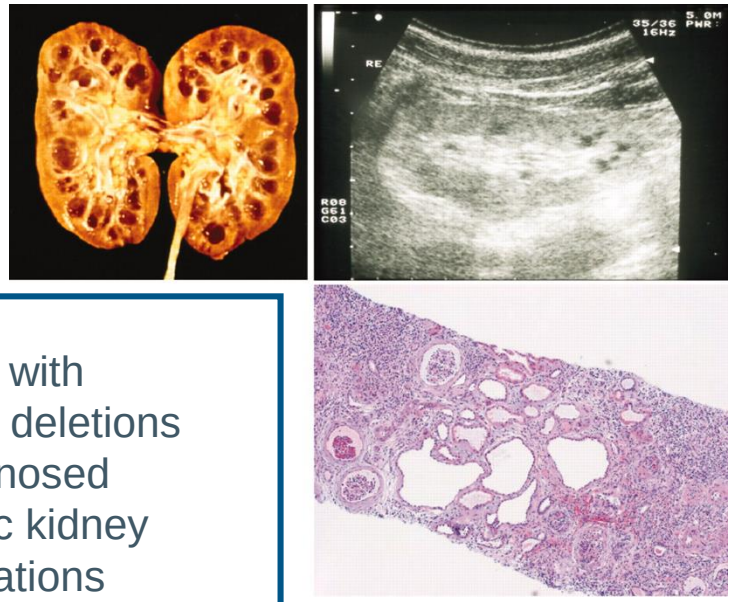
> Expansion of the 100,000 Genomes Project to **one million whole genomes** sequenced by NHSE and UK Biobank in the next five years

> From 2019, the NHS will offer **whole genome analysis for all seriously ill children with a suspected genetic disorder**, including those with cancer. The NHS will also offer the same for all adults suffering from certain rare diseases or hard to treat cancers

> An **aspiration to sequence 5 million genomes** in the UK within the next five-year years

Patient identification in rare disease

Case study: Nephronophthisis (NPHP)



- **Nephronophthisis (NPHP)** is a group of autosomal recessive renal diseases
- **Rare** with variable prevalence (1 in 50,000 in Canada, 1 in 100,000 in Finland, 1 in 922,000 in US)
- Most common genetic cause of End Stage Renal Disease (ESRD) in children and young adults
- Multiple genes associated with NPHP (up to 22)
- NPHP Type 1 is most common disorder, caused by total homozygous deletion of **NPHP1 gene**

- Identified 12 patients with homozygous NPHP1 deletions
- All previously undiagnosed
- At least 9 had chronic kidney disease with presentations consistent with NPHP
- Follow up includes scanning for additional patients and analyzing HES data to better understand disease history

Source: Hildebrandt & Zhou - JASN June 2007, 18 (6) 1855-1871; DOI: https://doi.org/10.1681/ASN.2006121344

What is the role of Orphan drugs in an increasingly segmented world?

	Today	Next 5 years	Next 10 years
Environment	• Value growth is highly concentrated into **specialty TAs** and developed country markets • **Stakeholder complexity grows**	• **Genetic profiling and biomarkers** create new payer propositions • Diseases are being divided and subdivided into smaller categories, treating **smaller sub-groups of patients**, with high per capita prices • **Patients increasingly activist**	• Markets radically re-defined by **genotype, biomarker** and other patient specific characteristics • **New payment models** for highly expensive products: payment by use, payment by outcome • **Regulatory process adapted** to accommodate advances in science and technology
Company	• New roles to adapt to **growing stakeholder complexity**	• **Post-marketing commitments** and RWI more frequently required	• Companies will be addressing unique value propositions by patient- the **"patient as CEO"** • Accurate **patient identification and diagnosis tools** developed

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