Rare Diseases - a BD view

In Pullan's Pieces #222, February 2026

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Rare diseases are a big growing market with huge unmet need.

Over 30M people in the US have a rare disease (FDA).

$190B in rare disease drug sales in 2024 says Research and Markets.

Approximately **44% of the clinical trial pipelines** in the U.S. and Europe are currently focused on orphan conditions. IQVIA 2024 R&D report

But only ~5% of ~70000 rare diseases have an approved drug!

Challenges of rare diseases for drug companies.

- Patients are rare, making clinical trial recruitment slow.
- Patients are often poorly diagnosed or diagnosed late.
- Rare diseases cross all therapeutic areas (making company interests variable and making searches and deal comps difficult).

- Patient access to expensive rare disease drugs varies by territory.

Governments have created incentives for "orphans", rare diseases that lack treatments.

An orphan disease is a governmental designation that refers specifically to rare conditions that lack sufficient research, funding, or commercial interest to develop treatments.

Region	Qualification Criteria	Benefits / Incentives
United States (FDA)	• <200,000 patients in the US, OR if >200,000, no reasonable expectation of recovering development costs	• 7 years market exclusivity • Tax credits for clinical trial costs • Waiver of FDA user fees • Eligibility for FDA research grants • Regulatory guidance/support
European Union (EMA)	• Prevalence ≤5 in 10,000 people in EU • Disease must be life-threatening or chronically debilitating • Either: no satisfactory treatment exists, or drug provides significant benefit • Or: unlikely to generate sufficient returns	• 10 years market exclusivity (can reduce to 6 if criteria no longer met) • Additional 2 years if pediatric studies completed • Fee reductions for regulatory procedures • Protocol assistance (scientific advice) • Centralized EU approval pathway
Japan (MHLW/PMDA)	• <50,000 patients in Japan • High medical need (no alternative or superior efficacy/safety) • Reasonable development plan required	• Extended re-examination period (functions as exclusivity) • Grant-in-aid for R&D • Tax deductions for R&D expenses • Priority consultation and review • Premium drug pricing
China (NMPA / evolving framework)	• No fixed prevalence threshold • Must treat a rare disease listed in the official Rare Disease Catalog • Must demonstrate significant clinical value	• Expedited review pathways • Priority regulatory review • Potential inclusion in National Reimbursement Drug List (NRDL) • No formal exclusivity framework yet • Incentives less structured compared to US/EU/Japan

Orphan exclusivity in the US, Japan and China protects only same molecule in the 1 indication. Europe protects against similar drugs in the same indication.

United States

The FDA cannot approve another drug for the same orphan indication during the 7 years of exclusivity, even if it's a different molecule or mechanism unless the competitor shows clinical superiority (greater efficacy, safety, or major contribution to patient care).

European Union

For 10 years, protects against approval of a similar (same principal molecule features or mechanism of action) medicinal product for the same orphan indication, unless the competitor is clinically superior or if the original product cannot be supplied in sufficient quantities.

Japan

Until the re-examination at 10 years (for orphan drugs), competitors cannot market drugs for the same rare indication. Exceptions exist if superiority is demonstrated.

China

China just revised its policy, providing 7 years of exclusivity for the same drug in the same indication. Initially this is for 12 indications listed in the Rare Disease Catalog.

There are also other governmental incentives

United States

Inflation Reduction Act (IRA) Exemption:
Orphan drugs with a **single orphan designation** are exempt from Medicare price negotiation under the IRA. However, if the drug later gains approval for non-orphan indications, it may lose this exemption and become subject to negotiation.

Exclusion of orphan drugs from MFN pricing

Rare Pediatric Disease Priority Review Voucher (PRV):
FDA grants a transferable voucher for drugs treating rare pediatric diseases. This voucher shortens FDA review time and can be sold (often for hundreds of millions of dollars). The program was recently reauthorized until September 2029.

Tropical Disease PRV Program:
Similar transferable vouchers exist for drugs targeting certain neglected tropical diseases

Other Incentives:
- Grants from NIH/FDA for rare disease research
- Waivers/reductions of FDA fees
- Priority regulatory guidance

European Union

Pediatric Extension:
Completing agreed pediatric studies can extend orphan exclusivity by **2 years** (from 10 → 12 years).

Fee Reductions:
EMA provides significant fee waivers for protocol assistance, marketing authorization, and inspections.

Centralized Approval Pathway:
Ensures pan-EU market access with one application.

Japan

Premium Pricing:
Orphan drugs often qualify for **premium reimbursement pricing** under Japan's national health insurance system.

Government Subsidies:
Grants-in-aid and tax credits for R&D costs.

Priority Consultation & Review:
Faster regulatory timelines through PMDA.

China

Rare Disease Catalog:
Drugs targeting conditions listed in the catalog receive expedited review.

NRDL Inclusion:
Priority consideration for reimbursement under the National Reimbursement Drug List.

Policy-Driven Incentives:
Less formalized than US/EU/Japan — exclusivity protections are

limited, but regulatory acceleration and reimbursement support are strong levers.

Top 20 Pharmas have Rare Diseases on their partnering wish lists

Among the top 20 pharma companies, Takeda and Boehringer Ingelheim (BI) list rare diseases as 2nd in their partnering wish lists (2nd to immunology for Takeda and 2nd to CV/metabolic for BI).

Amgen, Pfizer, AstraZeneca and Sanofi also list rare diseases in their wish lists on their partnering webpages or brochures.

Big companies generally built their rare disease franchises with deals and generally seek assets adjacent to their existing drugs.

Takeda: acquired **Shire** in 2019 for **$62B** adding assets for hereditary angiodema (HAE), lysosomal storage disorders, rare hematology Von Willebrand disease, rare CNS (pursued with its ADHD drug) and rare epilepsies, and rare GI diseases.

Takeda provides a wish list in rare diseases of

- rare hematology (hemophilia, Von Willebrand, thrombotic thrombocytopenia purpura),
- rare immunology (HAE, immune deficiency diseases,
- rare autoimmune diseases, hypoalbuminemia and hypovolemia, severe congenital Protein C deficiency, prothrombin deficiency, AATD, EoE, CIDP, MNM) and

- Lysosomal Storage Diseases (Hunter, Fabry, Gaucher. Post-transplant CMV)

Amgen: has long sought orphan drugs in oncology and hematology but with the **$28B Horizon Therapeutics** acquisition in 2023, Amgen added products for thyroid eye disease, neuromyelitis optica, and chronic refractory gout and a pipeline with ANCA-associated vasculitis and other rare inflammatory diseases.

AstraZeneca: acquired **Alexion** in 2021 for **$39B**. In 2025, AstraZeneca reported its rare disease focus contributed $58.7B in revenue in 2025. Alexion's complement inhibitors are key products.

Sanofi: acquired **Genzyme** in 2011 for **$20B** and the Genzyme portfolio in lysosomal storage diseases became the foundation of Sanofi's rare disease business.

Biogen: signed an option deal for Spinraza for SMA spinal muscular atrophy in 2012 from **Ionis Pharmaceuticals** for **$29M** upfront and **$270M** in milestones. Peak sales were $2B in 2019 and $1.5B in 2025. This deal provided the cornerstone for Biogen's rare disease franchise and validated antisense as an approach.

Today, Biogen says it seeks rare disease assets in

- CV,
- hematology,
- metabolic, and
- others with prevalence >=1/100,000 and with a clear path to patient identification and treatment.

Pfizer: built its own rare disease group 30 years ago and was successful with ATTR, transthyretin amyloid cardiomyopathy drug Vyndaqel. Although Pfizer sold its early gene therapy programs to Alexion/AstraZeneca, it has numerous hematology clinical stage programs for Tissue Factor hemophilia, hemophilia A and B, and sickle cell.

A sampling of rare disease companies outside the top 20.

Agios Pharmaceuticals- focusing on hemolytic anemias.

Alector - focused on frontotemporal dementia (FTD).

AliveGen - with an activin ligand trap for PAH, DMD, SMA or OI as well as big indications.

ANI Pharmaceuticals - rare diseases in rheumatology, nephrology, neurology, pulmonology, and ophthalmology.

Arcturus - has LNP delivery for gene medicines

Ascendis - delivery platform applied to rare endocrinology assets.

Athira Pharma - rare neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS).

Biomarin - enzyme replacement therapies, gene therapies, with 8 approved in achondroplasia, phenylketonuria, hemophilia, and mucopolysaccharidosis.

Biophytis - an activator of the MAS receptor in myocytes for DMD, also in trials for diseases of aging.

Bora Pharmaceuticals - rare pediatric neurology and children's epilepsy.

C4 Therapeutics -using targeted protein degradation to treat diseases, including multiple myeloma.

Chiesi Global Rare Diseases - a unit of Chiesi Group, includes lysosomal storage disorders like Fabry disease and alpha-mannosidosis.

CRISPR Therapeutics – using its gene-editing to develop therapies for both common and rare diseases, such as hemoglobinopathies.

Edgewise Therapeutics - rare neuromuscular diseases (e.g., Duchenne and Becker muscular dystrophy).

Fulcrum Therapeutics - genetically defined rare diseases, specifically hematologic disorders like Sickle Cell Disease.

Grace Therapeutics - rare and orphan diseases requiring novel drug delivery (e.g., aneurysmal subarachnoid hemorrhage).

Incyte- Jakafi for Polycythemia Vera (PV) as well as big indications.

Ionis Pharmaceuticals - with RNA targeting for hATTR amyloidosis, HAE , and neurology.

Invex Therapeutics - rare neurological and neurodevelopmental disorders (e.g., Fragile X Syndrome).

Ipsen - rare cholestatic-liver diseases, bone diseases, and endocrinology.

Jazz Pharmaceuticals - focus on rare sleep, rare epilepsy, and rare oncology therapeutic areas.

JCR - assets for Lysosomal storage disorders (LSD) and DMD

Kyowa Kirin - rare diseases requiring advanced antibody technology and hematopoietic stem cell gene therapy.

Merck KGaA - rare tumors (e.g., desmoid tumors and NF1-PN) and rare immunological diseases.

Mereo BioPharma Group - lead candidates for osteogenesis imperfecta (OI) and alpha-1 antitrypsin deficiency-associated lung disease (AATD-LD).

Moderna - a mRNA therapy for propionic acidemia in a registrational study.

PharmaEssentia- a drug for Polcythemia Vera (PV).

Pila Pharma - rare inflammatory and painful diseases (e.g., erythromelalgia).

PTC Therapeutics - particularly rare neurology and metabolism, with a marketed product for SMA.

Recordati - a business unit, Recordati Rare Diseases, for rare genetic metabolic disorders, endocrine diseases, and oncology.

Rezolute - developing ersodetug (RZ358) , an antibody designed to treat hypoglycemia caused by congenital hyperinsulinism.

Sarepta - in DMD and limb girdle muscular dystrophy (MGLD)

Shionogi - has made acquisitions to enter ALS, Pompe and Fragile X.

Shilpa Medicare - antibody targeting immune-evasion pathways in rare blood cancers like Essential Thrombocythemia.

Swedish Orphan Biovitrum – rare diseases in Specialty Care (genetic and metabolic) and hematology.

Tanabe Pharma - a program in ALS.

THX Pharma (Theranexus) - rare neurological diseases (e.g., Batten disease and Gaucher disease).

Travere Therapeutics - rare kidney and metabolic diseases , such as IgA nephropathy (IgAN) and focal segmental glomerulosclerosis (FSGS).

Ultragenyx Pharmaceutical - with approved drugs for X-Linked Hypophosphatemia (XLH) and Tumor-Induced Osteomalacia (TIO).

Vertex – pioneered in CF, has focus on Sickle Cell, and transfusion dependent thalassemia (TDT).

Viking Therapeutics - treatment of X-linked adrenoleukodystrophy (X-ALD).

Zevra Therapeutics – Niemann-Pick disease type C and metabolic diseases.

This is a diverse (incomplete) list-- from bigger companies pursuing rare diseases as a subset of other therapeutic areas, to companies applying a technology platform, to older names long focused on rare diseases to younger companies recognizing the need.

Many of the successful launches have been in Oncology or Monogenic rare diseases (below).

TA	Examples	Gene(s) Involved
Neuromuscular	Spinal muscular atrophy (SMA), Duchenne muscular dystrophy	SMN1, DMD
Metabolic	Gaucher disease, Fabry disease, Pompe disease, Tay-Sachs disease	GBA, GLA, GAA, HEXA
Hematology	Hemophilia A & B, sickle cell disease, beta-thalassemia	F8, F9, HBB
Endocrinology	Achondroplasia, congenital hypothyroidism	FGFR3, TSHR
Immunology	Severe combined immunodeficiency (SCID), chronic granulomatous disease	ADA, CYBB
Cardiology	Hypertrophic cardiomyopathy, familial hypercholesterolemia	MYH7, LDLR
Ophthalmology	Retinitis pigmentosa, Leber congenital amaurosis	RHO, CEP290

Recent rare disease approvals have significant sales forecasts.

Product	Company	Indications	Target	Modality	Sales(f) 2031 (GlobalData)
OJEMDA (tovorafenib)	Day One & Ipsen	Pediatric Low-Grade Glioma (LGG) and other tumors	BRAF kinase	Small molecule	**$765M**
REDEMPLO (plozasiran)	Arrowhead	Familial Chylomicronemia Syndrome (FCS), other chylomicronemias	ApoC-III	siRNA	**$1020M**
DUVYZAT (givinostat)	Italfarmaco	DMD, Becker MD, Crohn's, CLL	HDAC	Small molecule	**$597M**
ENJAYMO (sutimlimab)	Recordati/Sanofi	Acquired hemolytic anemia, ITP, kidney transplant rejection	Complement protein component 1, s	Antibody	**$431M**

Rare disease deals continue to illustrate the diversity of indications and modalities.

Rare Disease Acquisitions

- **BioMarin Pharmaceutical** - **Amicus Therapeutics** for **$4.8 billion** in December 2025 to expand its leadership in lysosomal storage disorders.
- **Recordati** finalized the acquisition of **Enjaymo** from **Sanofi** in November 2024 to strengthen its rare endocrine and metabolic portfolio.
- **ANI Pharmaceuticals** acquired **Alimera Sciences** in September 2024, adding the rare ophthalmology assets **ILUVIEN** and **YUTIQ** to its portfolio.
- **SERB Pharmaceuticals** completed the acquisition of **Y-mAbs Therapeutics** in September 2025 to bolster its rare oncology offerings with **Danyelza** .
- **Pharming Group** completed the acquisition of **Abliva AB** in March 2025, gaining the mitochondrial disease asset **KL1333**.

Strategic Licensing and Collaborations

- **THX Pharma & Biocodex -** Batten-1 & TX01 (Batten, Gaucher, Niemann-Pick) -$12M upfront, $173M total plus royalties
- **Biogen & Stoke Therapeutics** - zorevunersen (SCN1A-related diseases) – outside US, Canada and Mexico.
- **Gilead & Leo Pharma –** oral STAT6 program – up to $1.7B for global rights
- **Recordati & Moderna** - mRNA-3927 (Propionic Acidemia)- $50M upfront, near-term milestones of $110M

- **InSilico & Stemline**- ISM5043 (KAT6 inhibitor) – worldwide rights.

We hope to get a few deals done in this complex space. Great unmet need!