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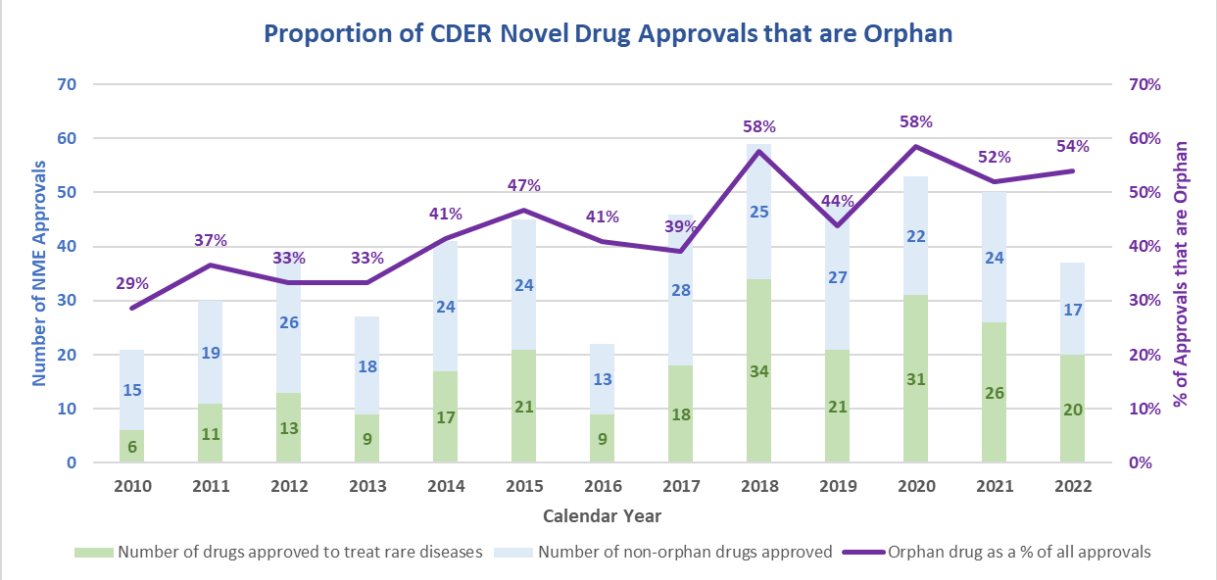
Supplementary information

De-risking rare disease acquisitions: a win–win–win for patients, biotech and investors

In the format provided by the authors

FDA approvals for rare disease drugs

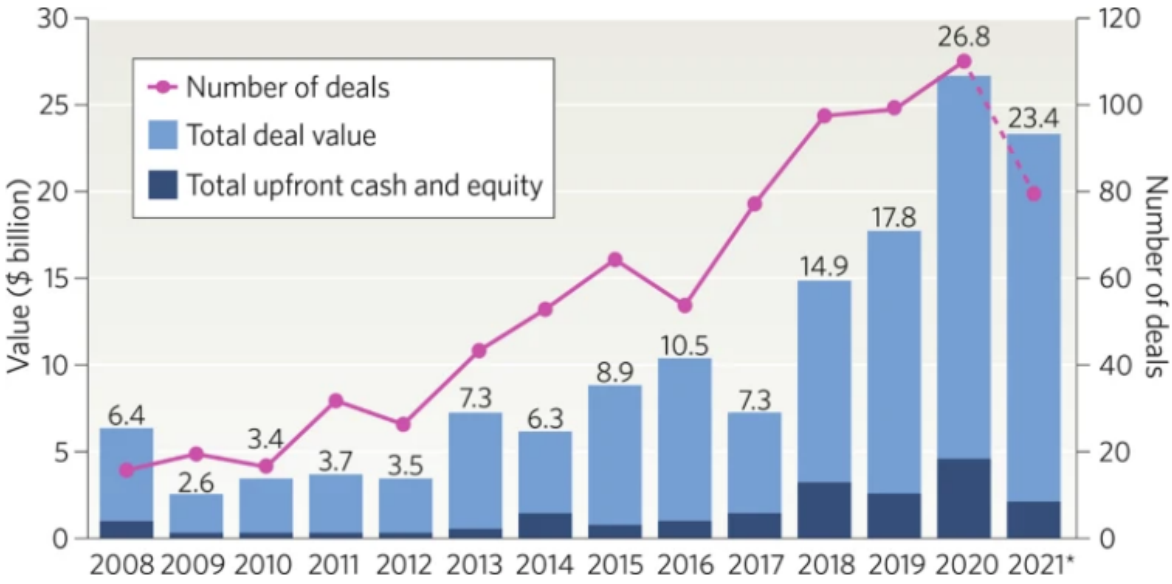
In the last 12 years, the proportion of approvals of novel drugs by the FDA's Center for Drug Evaluation and Research that are for rare diseases (that is, the drugs have orphan drug designation) has increased from 29% in 2010 to 54% in 2022 (Supplementary Figure 1).



Supplementary Figure 1 | **Proportion of CDER new drug approvals that are orphan drugs.** Data from 2010–2021[1] and 2022[2]. CDER, Center for Drug Evaluation and Research; NME, New Molecular Entity.

Partnerships related to rare diseases

The value of R&D partnership deals extracted from the DealForma database was $3.7 billion in 2011 and increased to more than $23.4 billion in 2021 (Supplementary Figure 2)[3].



Supplementary Figure 2 | **Annual rare disease R&D partnership activity[3].** Source: DealForma database. *Data for 2021 are up to 2 November.

M&A deals related to rare diseases
The total paid value at signing of rare disease M&A deals increased by 168%, from $18.9 billion in 2019 to $50.6 billion in 2022 (M. Daghlian, Global Genes, personal communication, 11 October 2023).

M&A deals involving rare diseases in the past 17 years were researched. This inquiry involved online exploration and extraction of relevant data. The dataset encompasses public M&A deals involving biotechnology and/or pharmaceutical companies. Primary sources utilized to retrieve information included press releases, company data and business news articles available online. The assembled dataset comprises the names of the acquired company (acquiree), the name of the acquiring entity (acquirer), some examples of rare diseases associated with the acquisition, the year of the acquisition and the source.

Risk in drug development for rare diseases
Rare disease investments are higher risk than mass-market drug development. The International Rare Diseases Research Consortium Chrysalis Task Force concluded[4] that "Overall, companies developing therapies for rare diseases perceive the different approaches of major regulatory agencies and limited early incentives for developing therapies for small populations as major challenges. This results in increased financial risk and uncertainty during drug development." Yates and Hinkel[5] agreed that the "moonshot" economics of rare disease development may make rare disease investment unfavourable.

Also, investors often focus their investment strategies on achieving FDA-approved treatments (time-to-market). However, the period from reaching the market following approval to achieving uptake in the clinic in rare disease therapy is fraught with additional risk. For example, each US state and payer has different policies as to which rare disease treatments gets reimbursed, to what degree and by whom. Similarly, each individual member state in the European Union has different policies for rare disease treatments.

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