Challenges of rare and ultra-rare diseases drug development: How to bridge the gap?

Kangaroo group, 22 November 2023

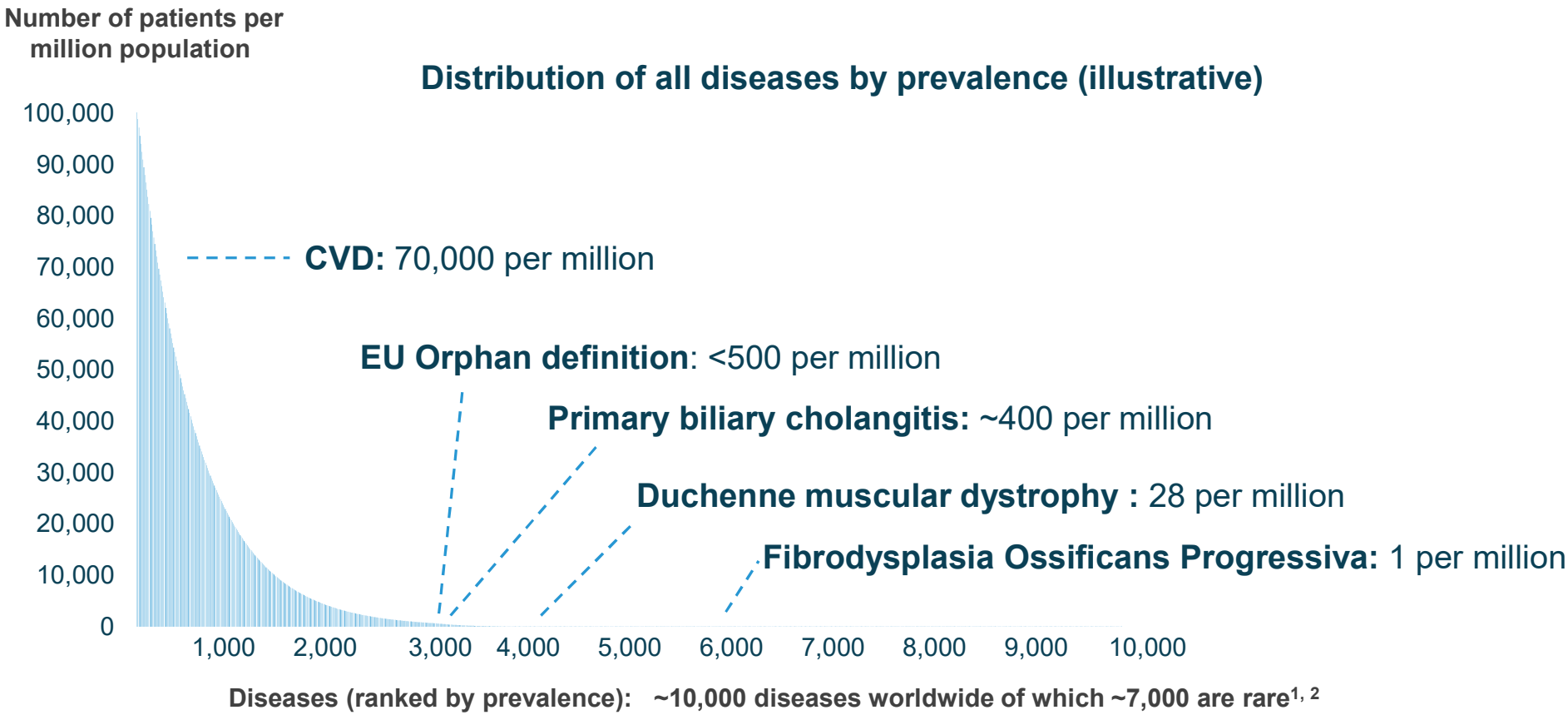
Martine ZIMMERMANN
Senior Vice-President, Global Head of Regulatory Affair at Ipsen

Choosing to ‘DO’ Rare Disease today

Savannah
Living with fibrodysplasia ossificans progressiva
Texas, USA

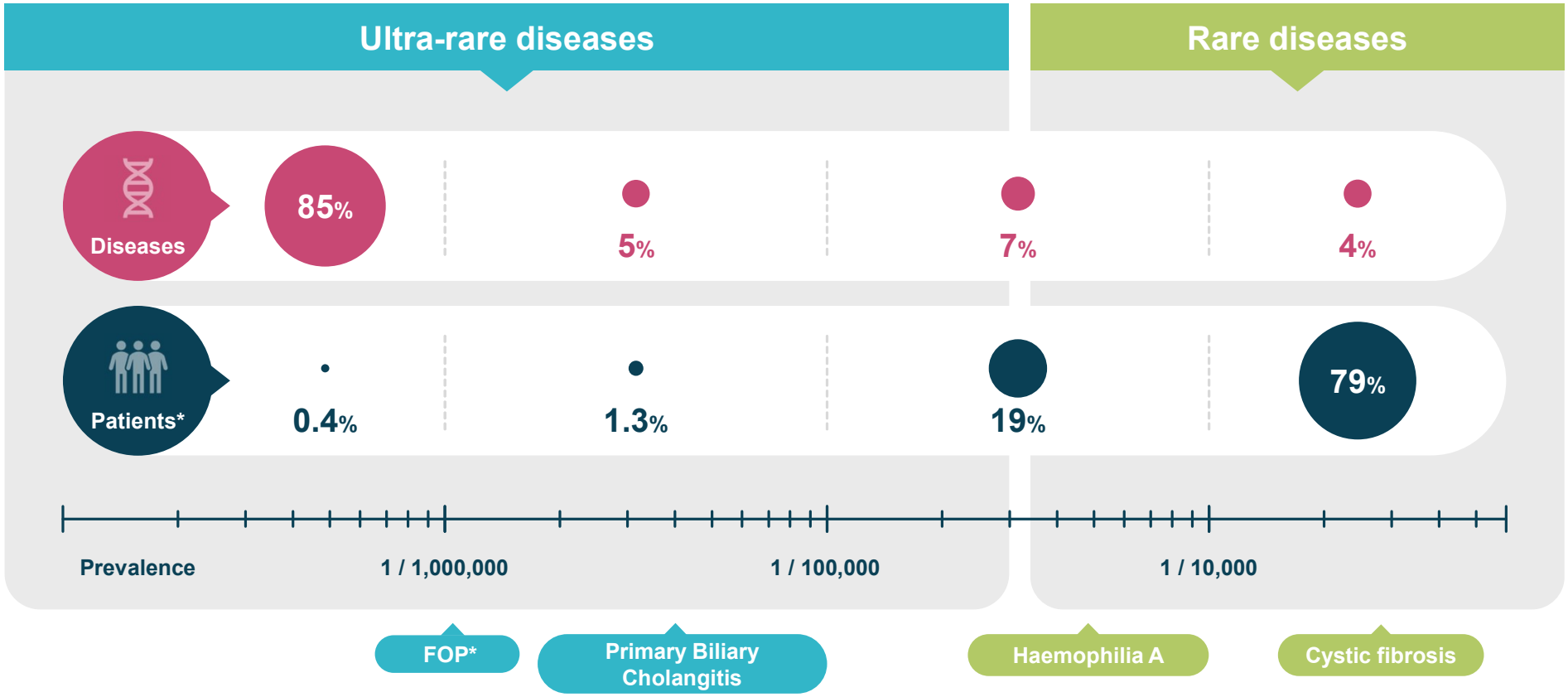
IPSEN
Innovation for patient care

What is **rare**?



References: 1. Milken Institute. Press release: Congress Passes 21st Century Cures Act, Bringing Forth New Era for Biomedical Innovation. 2016. Available from: https://milkeninstitute.org/article/congress-passes-21st-century-cures-act-bringing-forth-new-era-biomedical-innovation. 2. NORD. Rare Disease Day. 2019. Available from: https://rarediseases.org/wp-content/uploads/2019/01/RDD-FAQ-2019.pdf. 3. Kanth R, Shrestha RB, Rai I, VanWormer JJ, Roy PK. Incidence of Primary Biliary Cholangitis in a Rural Midwestern Population. Clin Med Res. 2017 Jun;15(1-2):13-18. Epub 2017 May 9

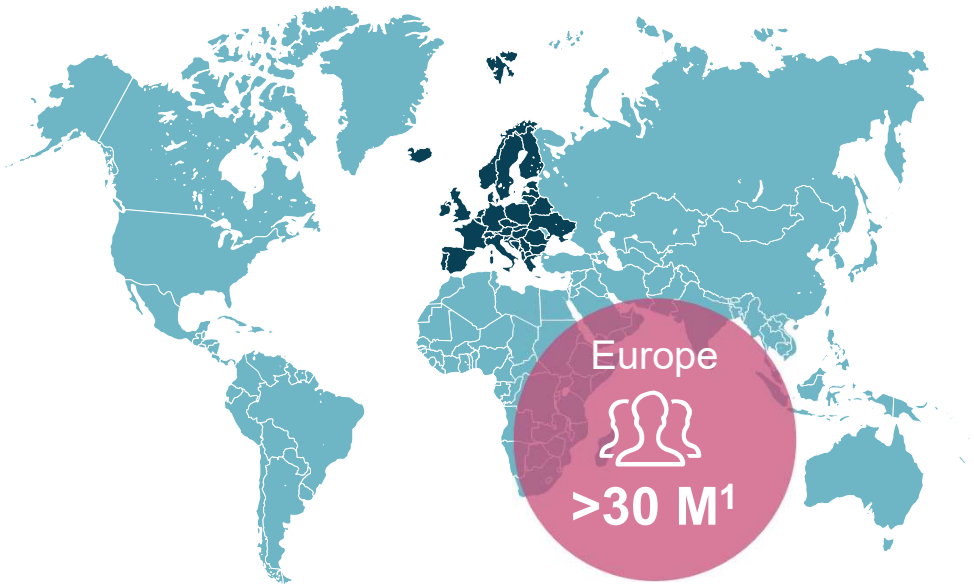
Ultra-rare diseases represent ~90% of rare diseases and affect less than ~15% of rare disease patients



*Average from range proportion of patients

Source: Wakap, S. N. *et al.* Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. *Eur. J. Hum. Genet.* **28**, 165–173 (2020).
*FOP – Fibrodysplasia Ossificans Progressiva

The *global* burden of rare diseases is high



>7,000 different rare diseases exist[1]

>300 million people worldwide[1]

~72% of rare diseases are genetic and most are chronic and life-threatening[1,2]

References: 1. Wakap SN, et al. Eur J Hum Genet. 2020;28:165–173. 2. Gülbakan B, et al. EPMA J. 2016;7(1):24.

Rare diseases tend to be **conditions with a high *individual* burden**

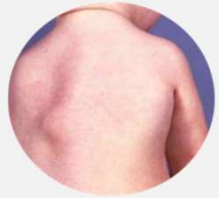
IPSEN Innovation for patient care

Source: Nicod, E. *et al.* Consideration of quality of life in the health technology assessments of rare disease treatments. *Eur. J. Heal. Econ.* 1–25 (2021).

Unmet need remains important across all types of rare diseases

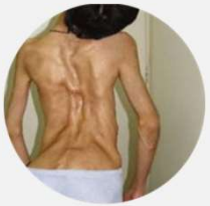
Fibrodysplasia Ossificans Progressiva

- **Ultra-rare**: ~1 / 1.14 million[1]
- **Severely debilitating** and disabling disease[1,2]
- Early childhood onset that considerably **shortens life expectancy** (~56 years)[3]



Nodule on back

Nodule on scalp



Ribbons

Primary biliary cholangitis

- **Rare:** 1 in 1,000 women[4]
- Often **asymptomatic** with significantly **lower quality of life**[4,5]
- Most present in **women aged 40-60**[4]

Worsening condition of the liver

References: 1. Baujat G, et al. Orphanet J Rare Dis. 2017;12:123. 2. Kaplan FS, et al. Best Pract Res Clin Rheumatol. 2008;22(1):191-205. 3. Kaplan FS, et al. J Bone Joint Surg Am. 2010;92(3):686-691
Images from Kitterman JA, et al 2012 Image (4) Provided by Dr. Genevieve Baujat. 4. Wakap SN, et al. Eur J Hum Genet. 2020;28:165–173. 5. Gülbakan B, et al. EPMA J. 2016;7(1):24.

Their unique nature comes with **unique clinical challenges** for the development of medicines

Rare diseases

Nature
- ⚠ Small, often young, heterogeneous, and geographically dispersed populations

Expertise
- ⚠ Limited disease knowledge (Natural History Studies, defined endpoints,…)
- ⚠ Lack of experts and patient organisations

Pathways
- ⚠ Poorly established standards of care
- ⚠ Insufficient diagnostic capabilities

Challenges

Pre-clinical development — e.g. unknown targets

Clinical development — e.g. small, uncontrolled trials

IPSEN Innovation for patient care

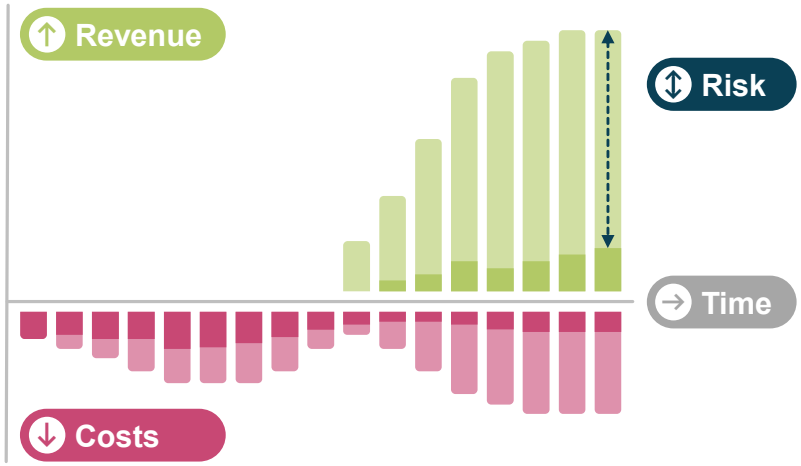
Source: Richter et al. Characteristics of drugs for ultra-rare diseases versus drugs for other rare diseases in HTA submissions made to the CADTH CDR. OJRD 2018; 13:15
Nicod et al. HTA programme response to the challenges of dealing with orphan medicinal products: process evaluation in selected European countries. Health Policy 2019;123(2),140-51
Neez et al. Addressing unmet needs in extremely rare and paediatric-onset diseases: how the biopharmaceutical innovation model can help identify current issues and find potential solutions.

These lead to **greater economic challenges and higher risk** for the development and commercialisation of medicines for ultra-rare diseases

Rare diseases

- ⚠ Small (uncertain) patient populations
- ⚠ High (per patient) cost of development / commercialisation
- ⚠ Greater risk of failure

Risk-adjusted Net Present Value (rNPV) model



Investment decisions

Source: Neez E., Gentilini A., Hutchings A. Addressing unmet needs in extremely rare and paediatric-onset diseases: how the biopharmaceutical innovation model can help identify current issues and find potential solutions. *Prepared by Dolon Ltd.* (2021) Available at: https://dolon.com/dolon/wp-content/uploads/2021/07/Addressing-unmet-needs-in-extremely-rare-and-paediatric-onset-diseases.pdf

Challenges of rare diseases drug development

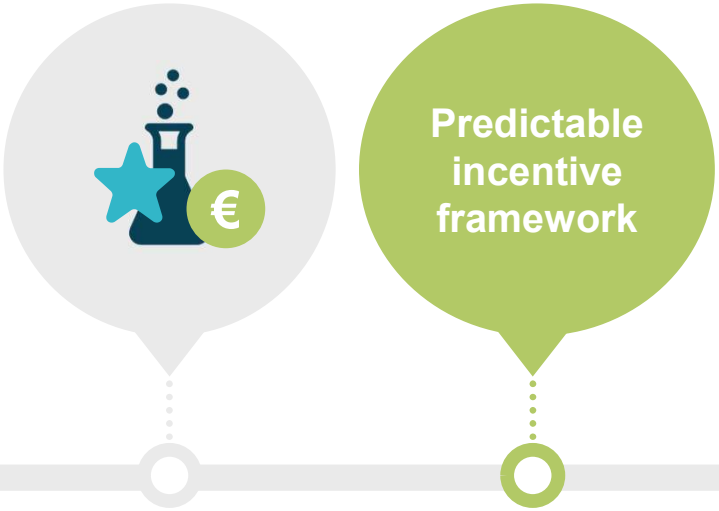
How to bridge the gap?

There is an urgent need for change to ensure that rare and ultra-rare innovation is rewarded, sustainable, and gets to the patients in need

1 R&D | 2 Regulatory | 3 Access

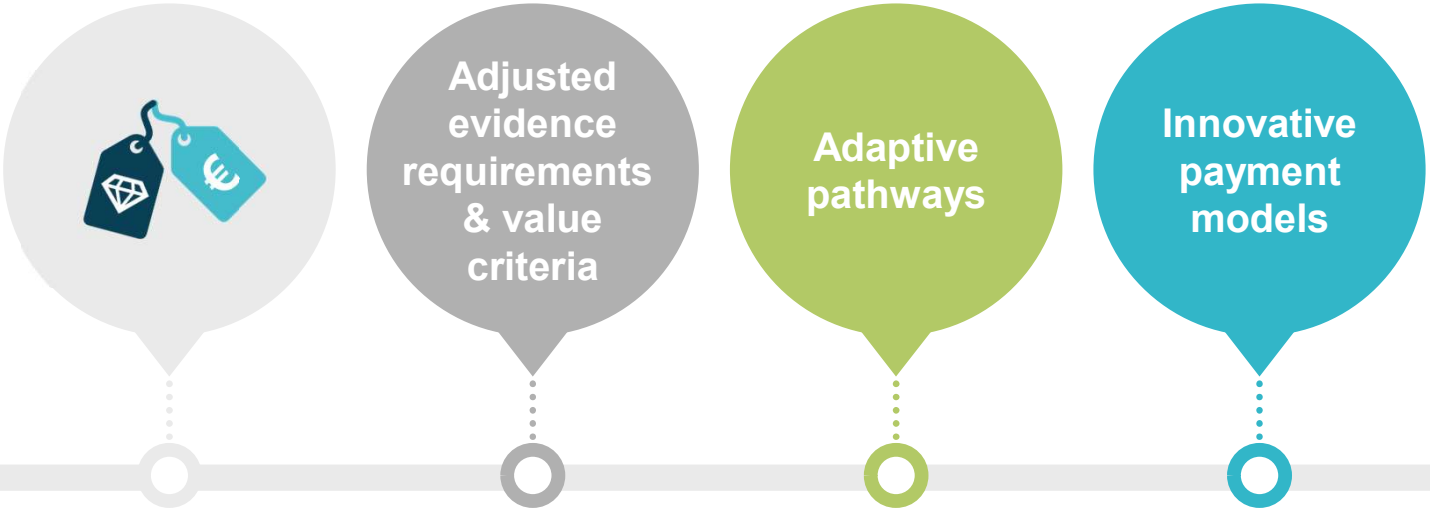
There is an urgent need for change to ensure that rare innovation is rewarded, sustainable, and gets to the patients in need

1 R&D | 2 Regulatory | 3 Access



There is an urgent need for change to ensure that rare and ultra-rare innovation is rewarded, sustainable, and gets to the patients in need

1 R&D | 2 Regulatory | 3 Access



EU Orphan legislation has driven innovation in rare diseases

Clear need

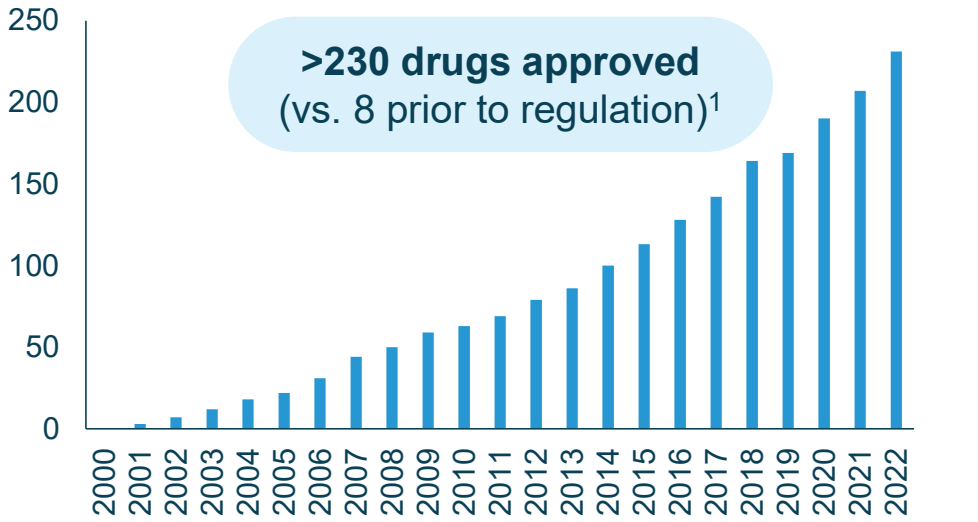
*Patients suffering from **rare** conditions should be **entitled to the same quality** of treatments **as other patients..***

*…It is therefore **necessary** to **stimulate research, development** and bringing to market **appropriate medications** by the pharmaceutical industry*

- EU regulation (2000) on orphan drugs[1]

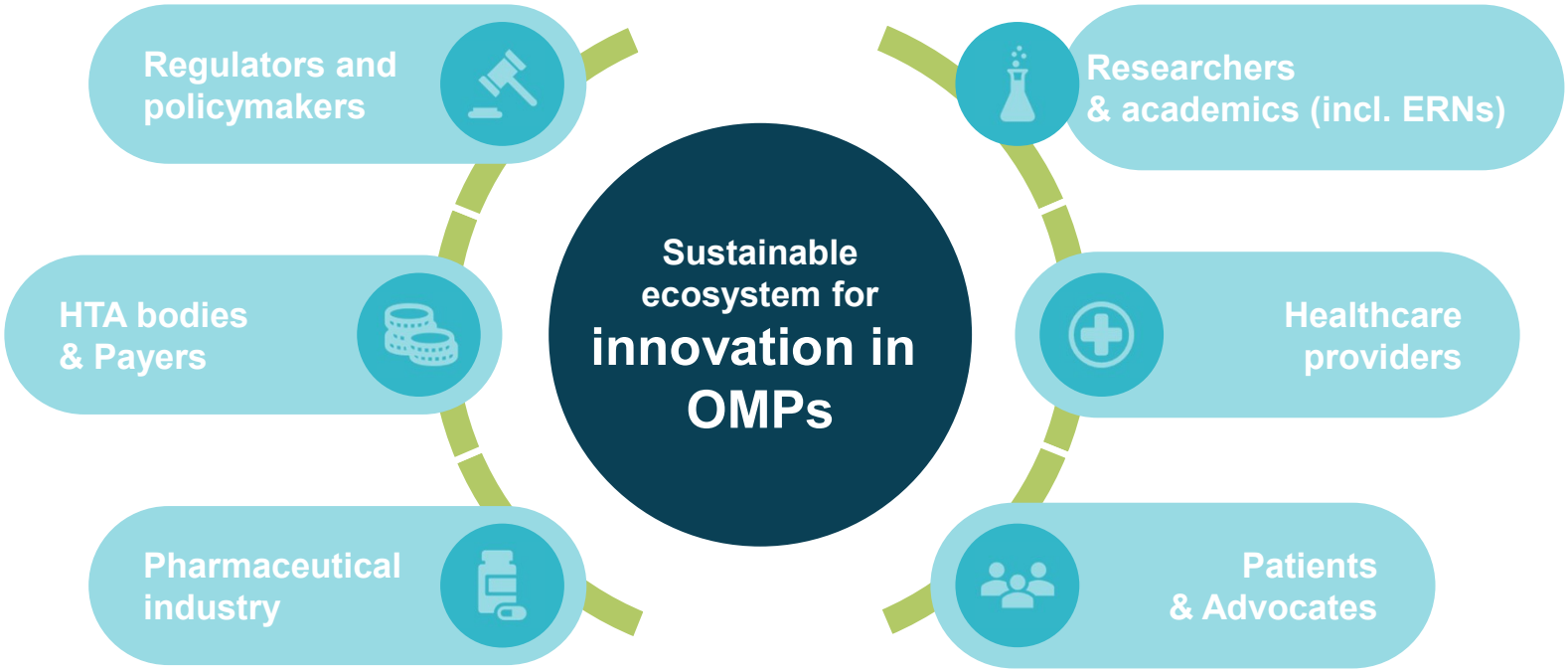
Clear impact

Cumulative OMPs approved in Europe 2000 - 2022[2]



References: 1. Orphan medicines in the EU. EMA, 2022; EMA 2023

We all need to **work together and do our part** to ensure that rare disease patients get the treatments they urgently need



Developing therapies for rare diseases is not easy

but …

It is undoubtedly the right and fair thing to do

Thank you