UMC Utrecht Wilhelmina Kinderziekenhuis

ICAT Innovation Center for Advanced Therapies

Prinses Máxima Centrum kinderoncologie

Internationale markt en toekomst: noodzaak tot samenwerking

Eduard J. van Beers

UMC Utrecht

U-TRIAL WE CONNECT

Symposium 030 januari 2025
Innovatieve therapieën bij kinderen - kan het slimmer en sneller?

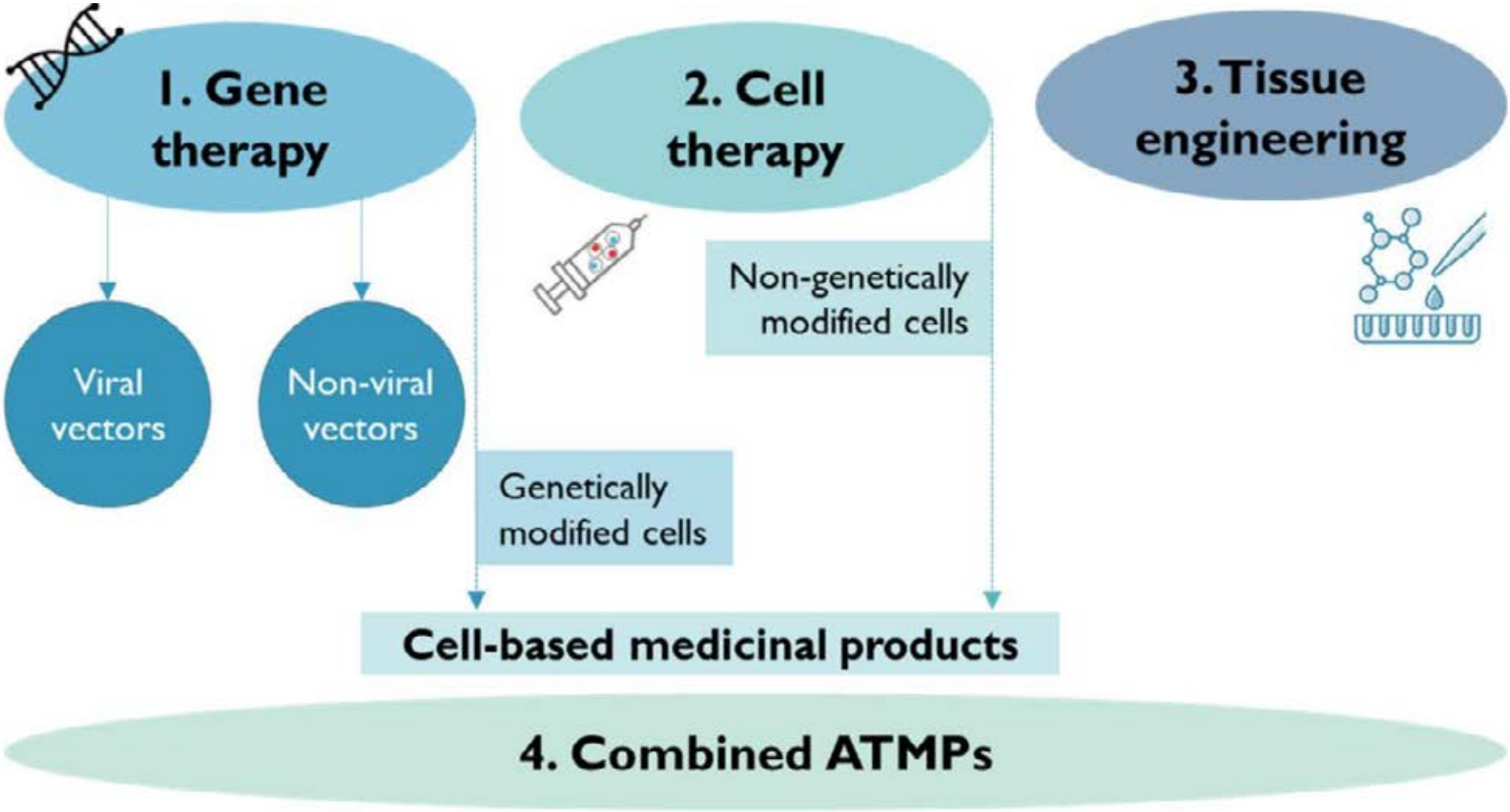
Conclusie

Innovatieve therapie in kinderen:

- Unmet clinical need in kindergeneeskunde is enorm
- Activiteit op het gebied van innovatieve therapie is enorm en groeit vooral in China
- Bij elke ontwikkelings stap gaan er initiatieven verloren
- Slecht een handvol ATMPs goed gekeurd elk jaar
- Nog minder wordt vergoed
- Lange doorlooptijden contracteren en regelgeving zijn een bottle-neck voor klinische ontwikkeling in EU
- Maar de markt groeit en dat geeft kansen

1990

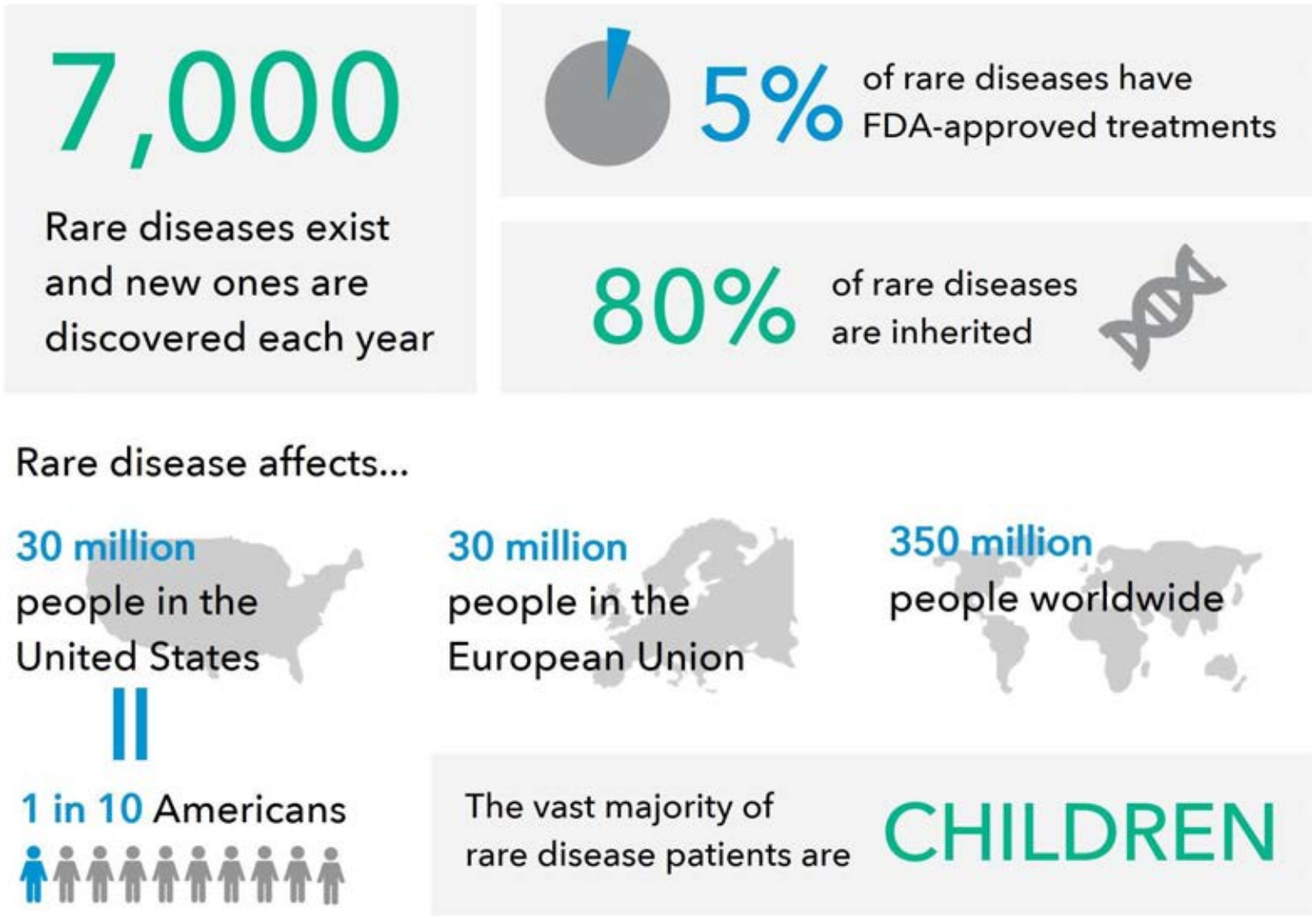
Advanced Therapy Medicinal Products (ATMPs)



Pharmaceutics.2023 Oct 6;15(10):2431.

In the EU: Regulation 1394/2007 of 13.11.2007

Patiënten waarvoor ATMPs ontwikkeld worden



From: www.chisite.org/blog/equitable-access-to-rare-disease-therapies-workshop
Center for Healthcare innovation

ATMP/RNA (11)

Gene
beremagene geperpavec
delandistrogene moxeparvovec
valoctocogene roxaparvovec

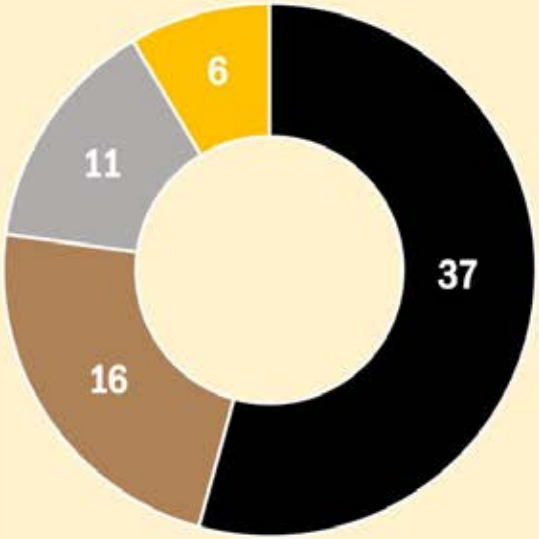
RNA
avacincaptad pegol
eplontersen
nedosiran
tofersen

Cell
donislecel
exagamglogene autotemcel
lovotibeglogene autotemcel
Vowst

Vaccines (6)

Abrysvo
Arexvy
Cyfendus
Ixchiq
Penbraya
Qdenga

EMA, FDA, MHRA
2023



Small Molecules/Peptides (37)

bexagliflozin
capivasertib
elacestrant
fezolinetant
fruquintinib
gepirone
ivosidenib
lotilaner
motixafortide
nirogacestat
palovarotene
pirtobrutinib
repotrectinib
ritlecitinib
sparsentan
taurolidine+heparin
vadadustat
zavegepant
zuranolone
birch bark triterpenes
daprodustat
etrasimod
flotufolastat F 18
gefapixant
iptacopan
leniolisib
momelotinib
nirmatrelvir+ritonavir
omaveloxolone
perfluorhexyloctane
quizartinib
rezafungin
sotagliflozin
sulbactam+durlobactam
trofinetide
vamorolone
zilucoplan

Antibodies/Proteins (16)

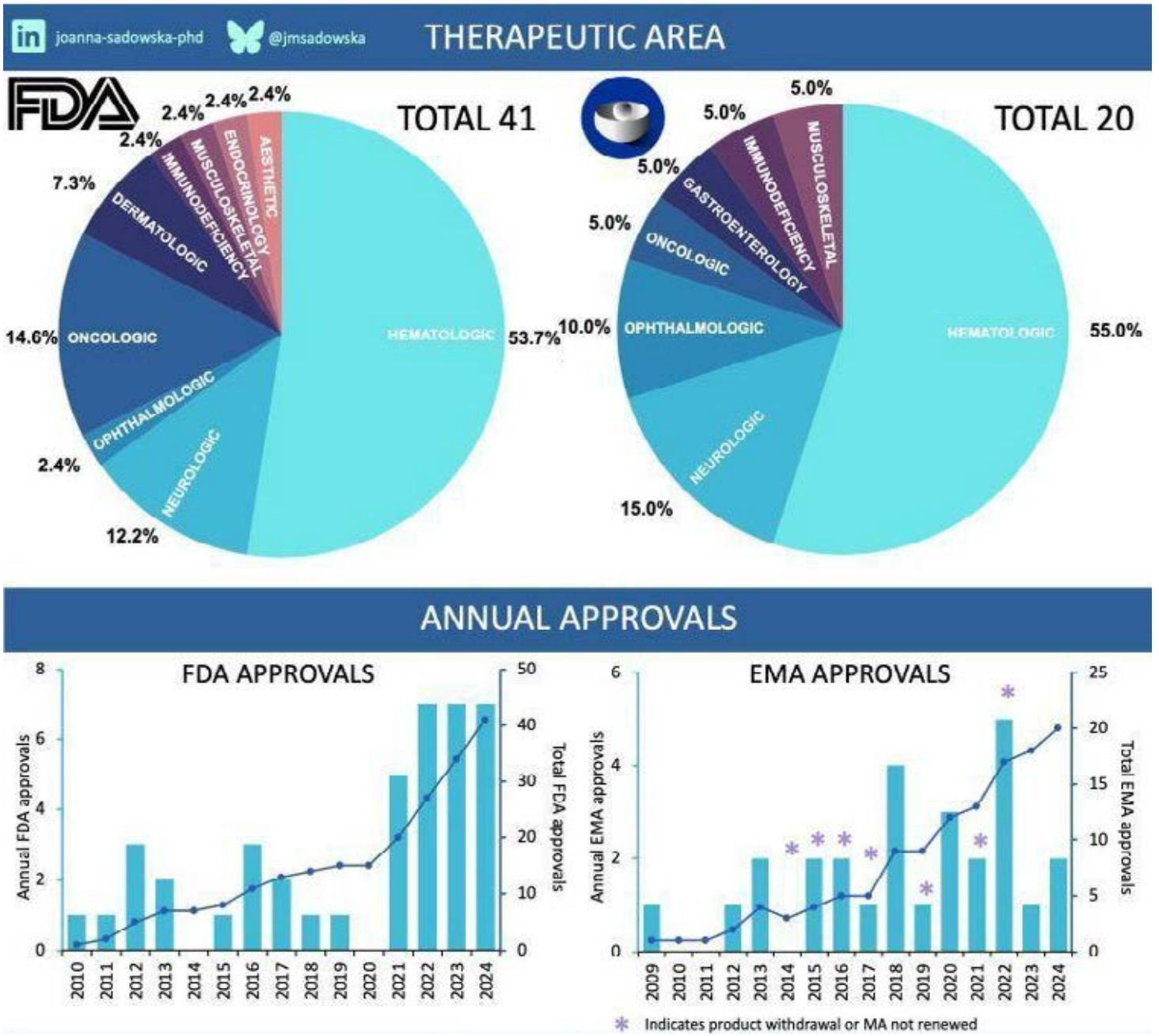
Human Proteins
efbemalenograstim alfa
pegzilarginase
Prothrombin Complex Concentrate

Antibodies
bimekizumab
lecanemab
nirsevimab
rozanolixizumab
toripalimab
lebrikizumab
mirikizumab
retifanlimab
tislelizumab

Bi-specific Antibodies
elranatamab
glofitamab
epcoritamab
talquetamab

Novel drugs approved by the EMA, the FDA, and the MHRA in 2023: A year in review
Br J Pharm. Volume181, Issue11 June 2024 P1553-1575 https://doi.org/10.1111/bph.16337

CELL AND GENE THERAPIES IN THE US AND EUROPE



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Programma: the ATMP lifecycle

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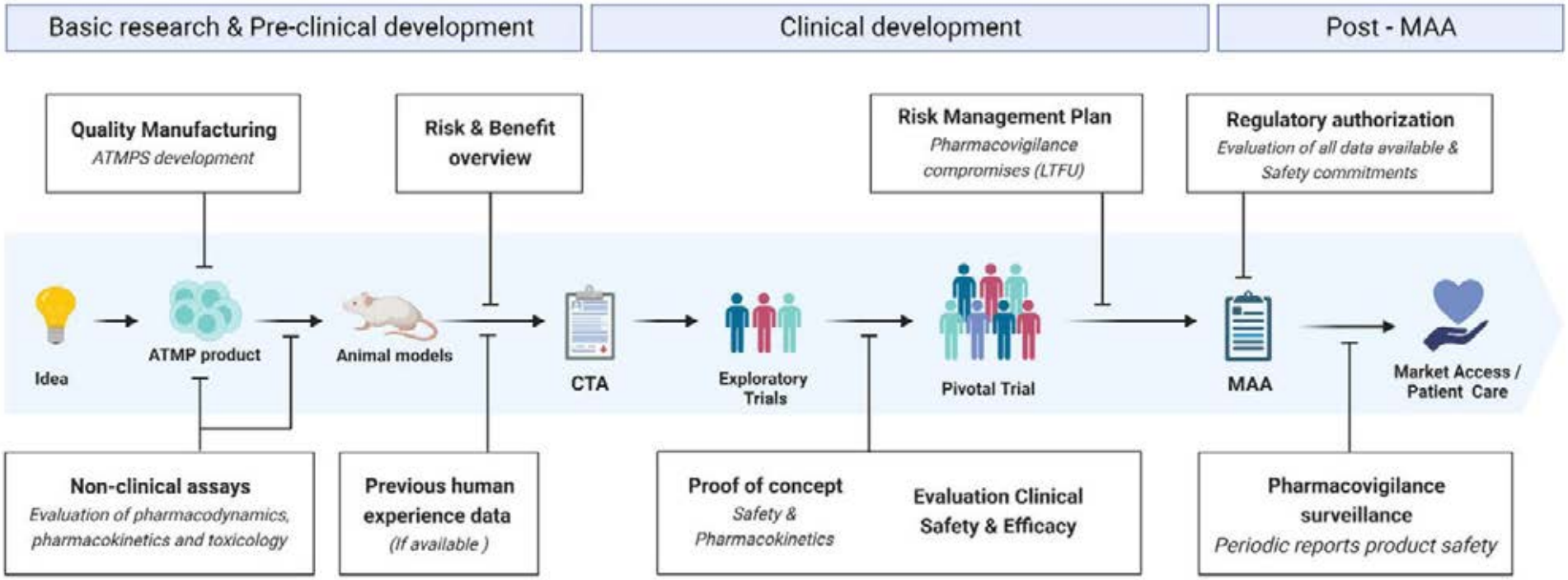

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Gen en celtherapie pipeline ontwikkeling

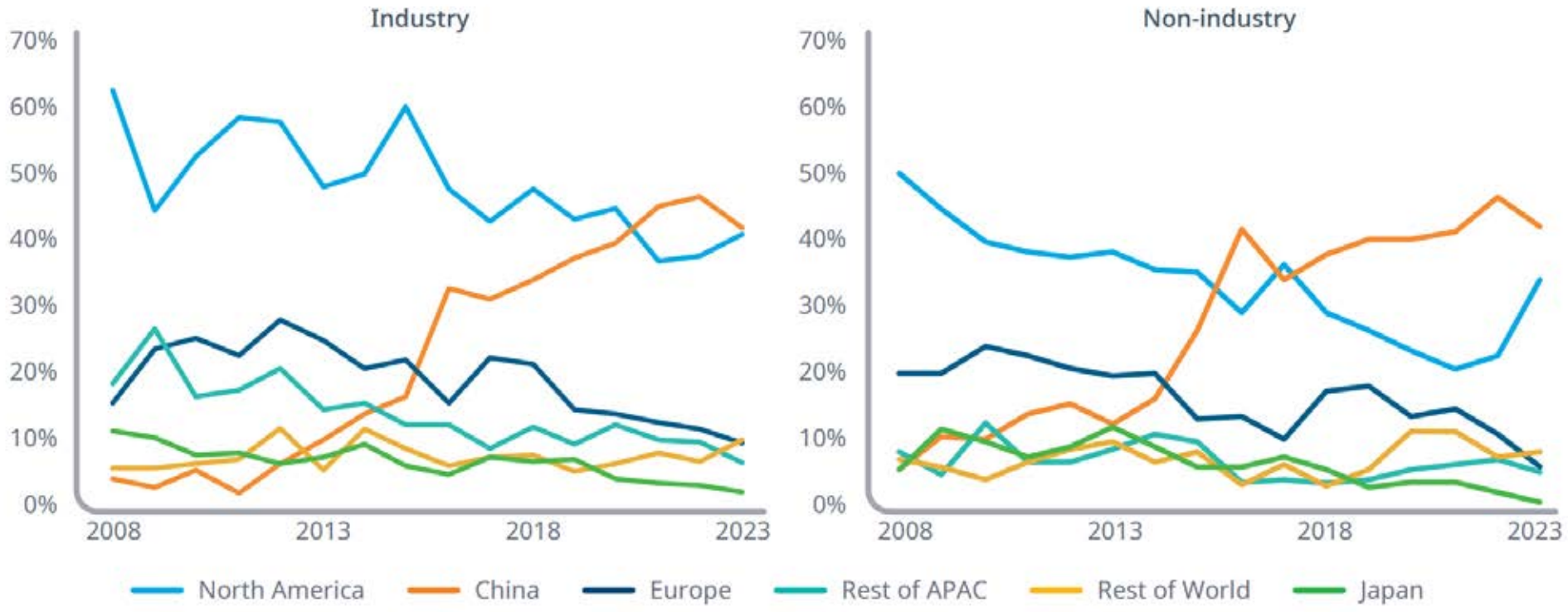
Global Status	Q3 2023	Q4 2023	Q1 2024	Q2 2024	Q3 2024
Preclinical	1,522	1,528	1,471	1,436	1,393
Phase I	256	270	301	314	318
Phase II	267	274	282	279	289
Phase III	30	33	35	34	35
Pre-registration	7	6	4	5	6
Total	**2,082**	**2,111**	**2,093**	**2,068**	**2,041**

CITELINE a norstella company

ASGCT American Society of Gene + Cell Therapy

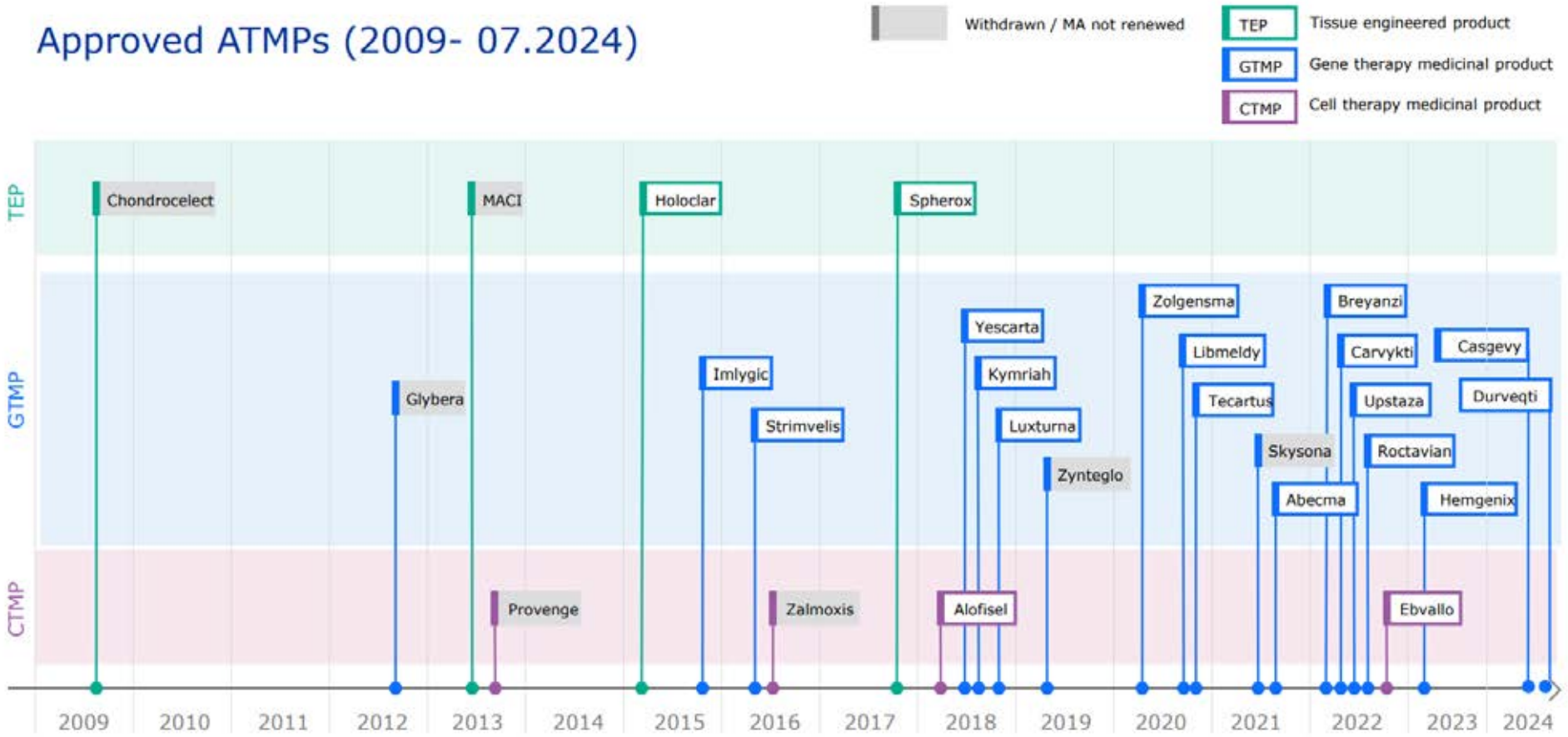
Gene, Cell, + RNA Therapy Landscape Report, American Society of Gene & Cell Therapy and Citeline, 2024 Q3
Original report source at https://asgct.org/publications/landscape-report

Cel en gen- therapie trials per regio



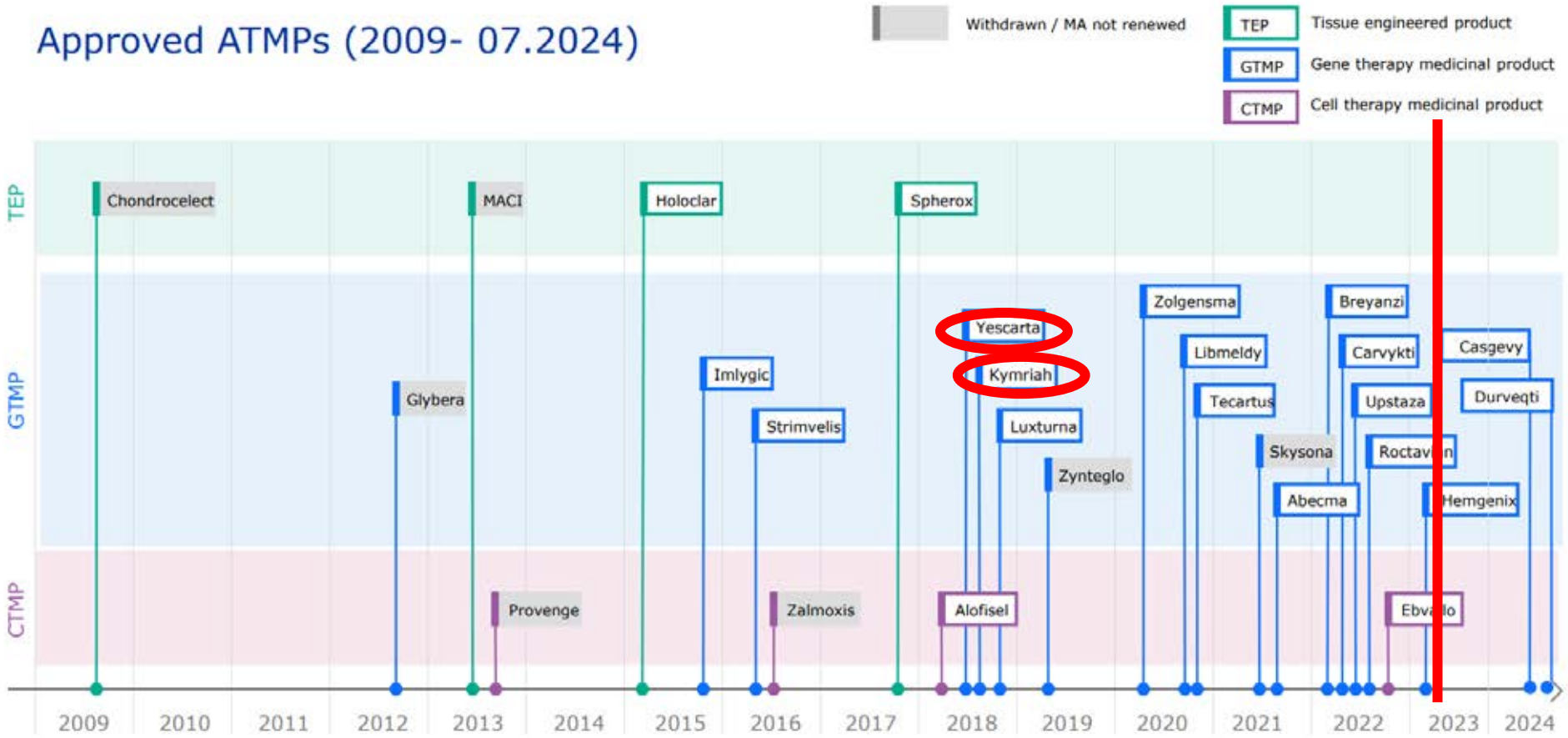
Source: Citeline Trialtrove, Dec 2023; IQVIA Institute, Jan 2024.

EMA goed gekeurde ATMPs



https://doi.org/10.1016/j.jval.2022.07.004

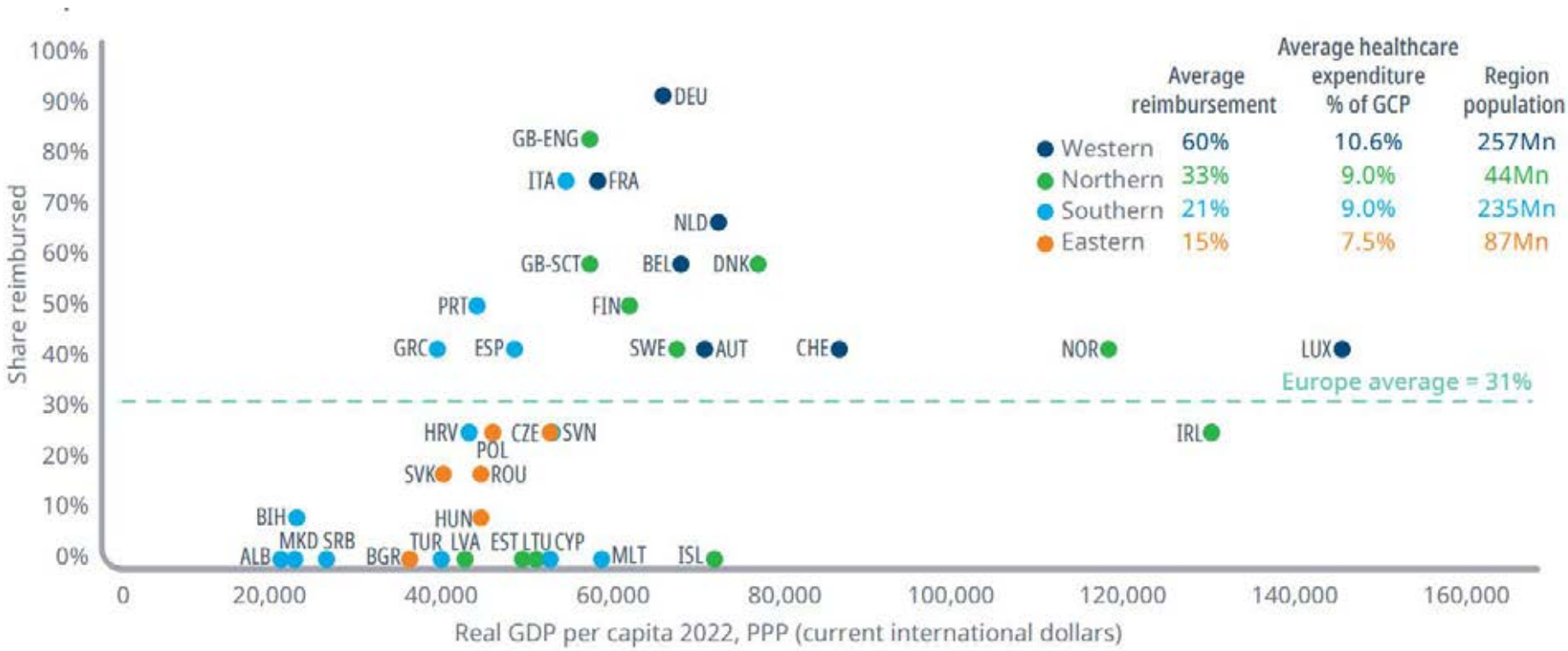
ATMPs: high financial and evidentiary uncertainty for regulators and payers



https://doi.org/10.1016/j.jval.2022.07.004

Status van cel en gen- therapie vergoeding in Europa

(Apr 2023)



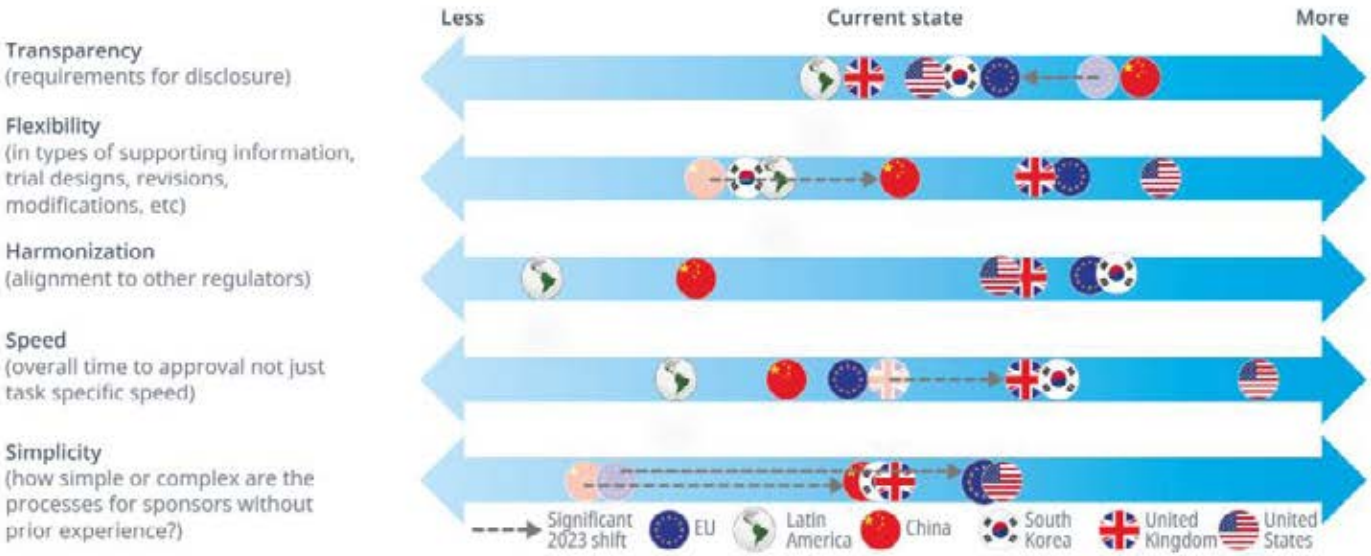
Source: European Medicines Agency, IQVIA EFPIA Patients W.A.I.T. Indicator 2022 Survey, Apr 2023; International Monetary Fund, Oct 2023; IQVIA Institute, Jan 2024.

Bureaucratie, veel regels lange doorloop tijden in EU

Variable regulatory environment

Global regulatory agency characteristics continue to differ across geographies

Comparative analysis of key characteristics of global pharmaceutical regulatory agencies



Median Start-up times 2024*:

- APAC: 322 days
- EMEA: **381 days**
- NA: 213 days

*Approved for Site Selection Visit to Site Activation, Top 80%

Source: IQVIA Clinical Trial Regulatory Management expert input, IQVIA Institute Jan 2024.
Report: Global Trends in R&D 2024: Activity, Productivity, and Enablers. IQVIA Institute for Human Data Science, February 2024.

What the EU is doing:

Set up and support:

- the European Reference Networks (ERNs)
- IT platform for consultation : the Clinical Patients Management System 2.0 (CPMS 2.0)
- the European Platform on Rare Disease Registration (EU RD Platform)
- the definition, codification and inventory of rare diseases (Orphanet)
- support the designation and authorization of **orphan medicinal products and PRIME programme**
- enhance making rare diseases registries and data FAIR
- International Rare Diseases Research Consortium (IRDiRC)
- empower patient organisations
- promote the development of national rare diseases plans and strategies
- ACT EU: (U-TRAIL advisory role: trial design, harmonization)
- R&D programme

https://health.ec.europa.eu/rare-diseases-and-european-reference-networks/rare-diseases_en#:~:text=In%20the%20EU:%201%20between%2027%20and%2036,5%2070%%20of%20rare%20diseases%20start%20in%20childhood

Research and development programme

- 2007 - 2020, >€3.2 billion:

- the Seventh Framework Programme (FP7)
- Horizon 2020
- Horizon Europe (2021-2027)

- public-private projects such as Conect4Children (Pedmed) or SCREEN4CARE, which are key to bring solutions for rare disease patients.

- Oct 2024: European Partnership on rare diseases (ERDERA):
- EUR 350 million for networking advocacy and grants in rare diseases

(= 0,028% of EU health expenditure/y: 1.221.000.000.000,00 euro)

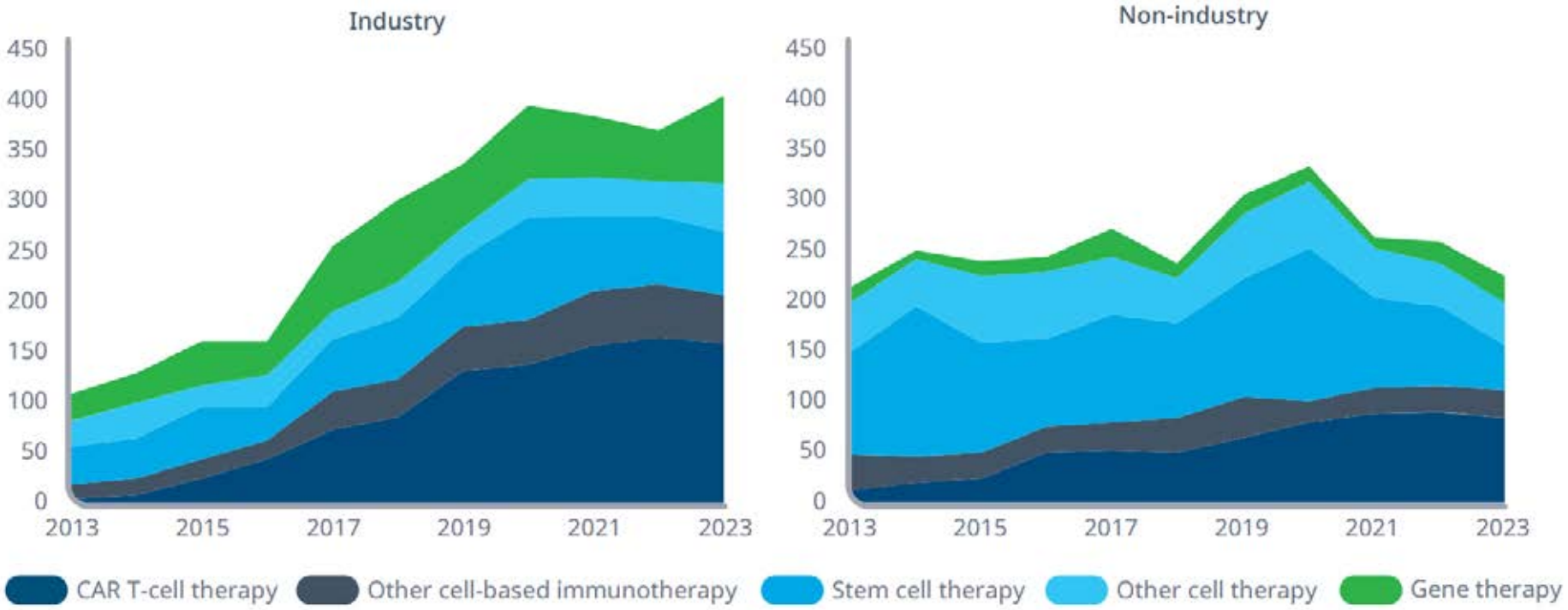
https://health.ec.europa.eu/rare-diseases-and-european-reference-networks/rare-diseases_en#:~:text=In%20the%20EU:%201%20between%2027%20and%2036,5%2070%%20of%20rare%20diseases%20start%20in%20childhood

Markt beweegt richting ATMPs

TREND TOWARD PRECISION MEDICINE

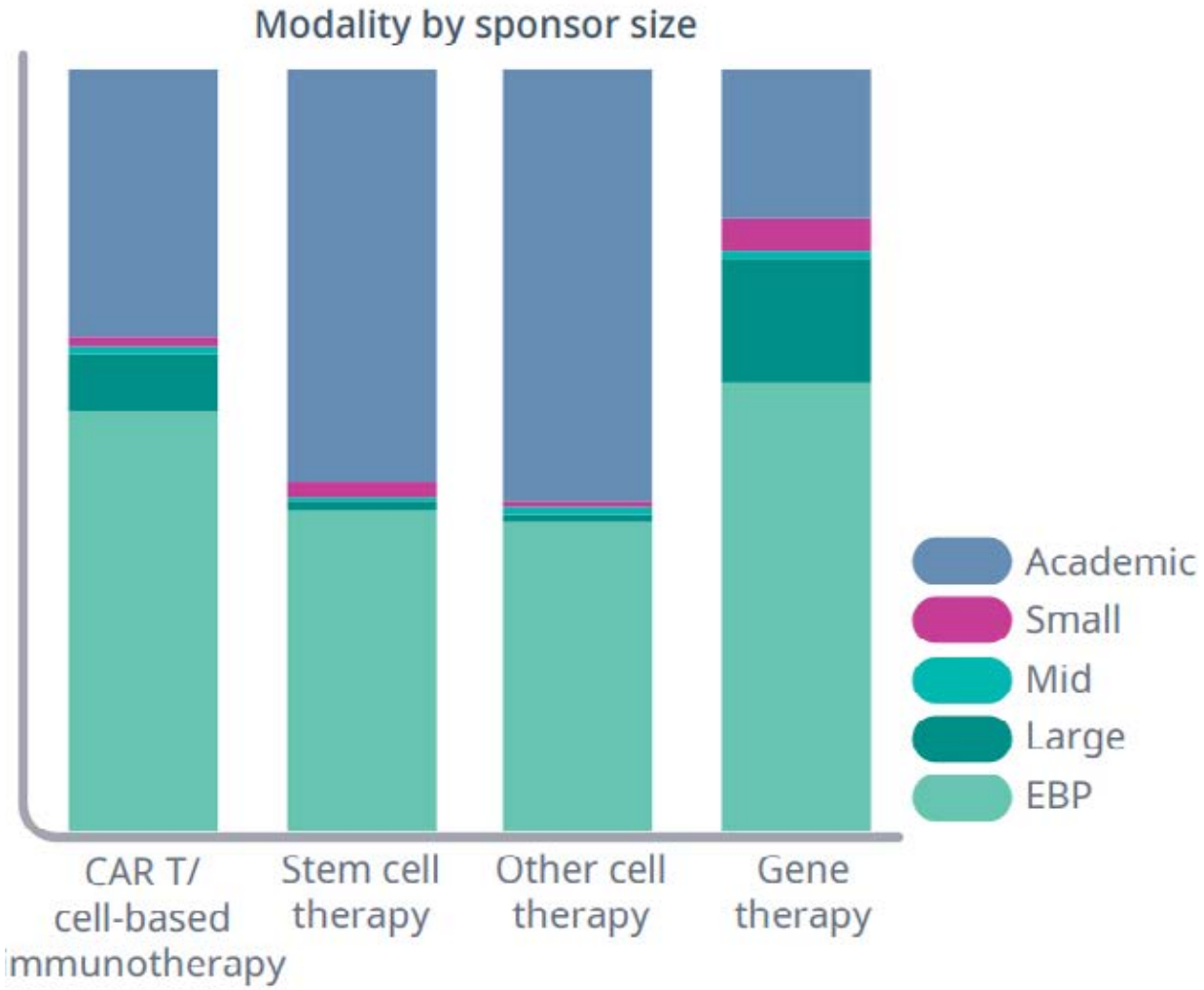
https://www.linkedin.com/pulse/breakthrough-evolving-beyond-blockbuster-drugs-john-neal-2jnqc/?trackingId=PpG2m63uRcSGKRRyh1YcBA%3D%3D

Amount of cell and gene therapy clinical trials grows



Source: Citeline Trialtrove, Dec 2023; IQVIA Institute, Jan 2024.

Trials met cel- en gentherapie op basis van bedrijfsgrootte



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Vooruitzicht ATMPs

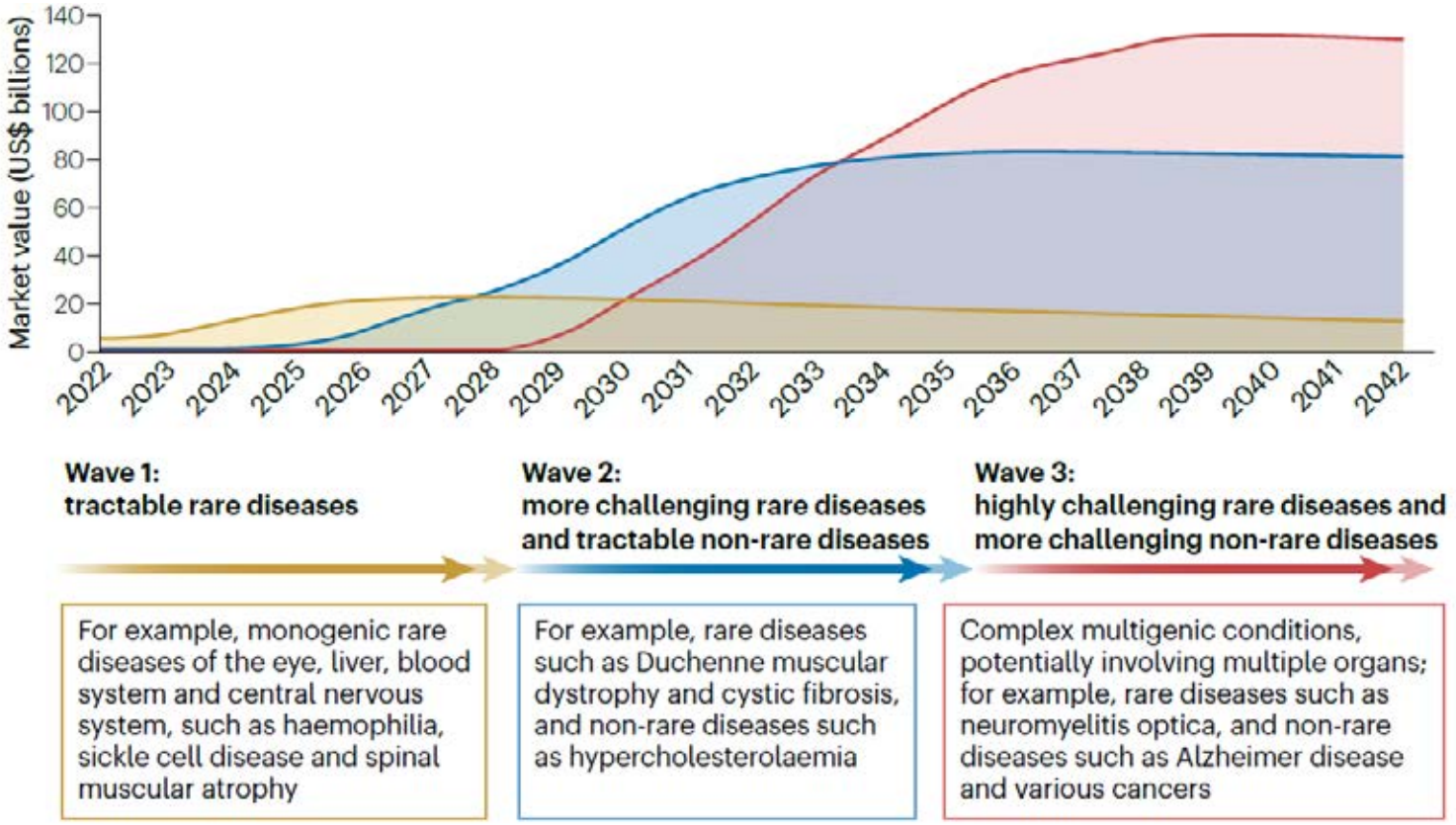

Fig. 2 | Market forecast for three waves of genomic medicines. Based on our analysis, we anticipate that there could be three waves of genomic medicines in the next two decades, driven by therapeutic tractability of different types of diseases and advances with technology platforms. See Supplementary information for details.

nature reviews drug discovery

Xie et al. Nat Rev Drug Dis sept 2023; vol 22:691-2

Conclusie

Innovatieve therapie in kinderen

- Unmet clinical need in kindergeneeskunde is enorm
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- Pannel discussies:
  - verdieping uitdagingen en oplossingen:

- wat kunnen wij doen?

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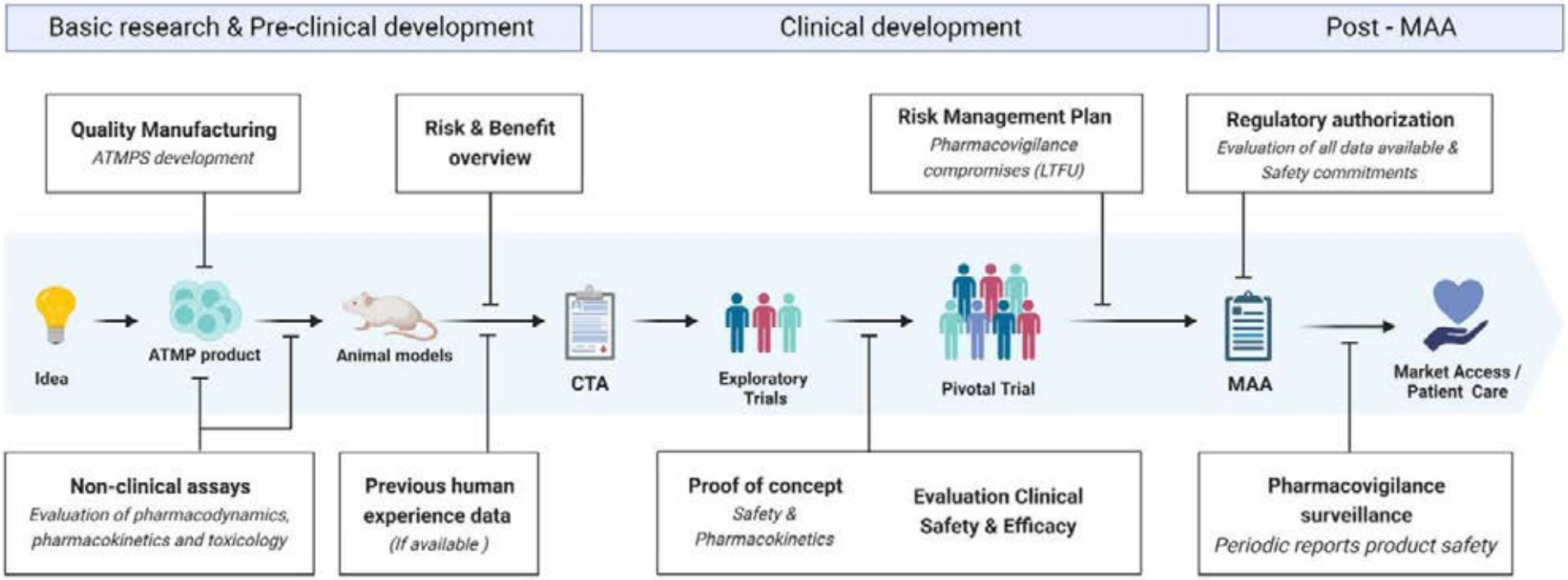

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Panel discussies: oplossings richtingen