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Highlights on the Committee for Advanced Therapies Joint PCWP-HCPWP session, 15th November 2023

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Committee for Advanced Therapies
European Medicines Agency

DISCLAIMER

Consultancy role for the pharmaceutical company Roche in the development of the product Evrysdi® (Risdiplam).

EU regulatory framework for Advanced Therapy Medicinal Products (ATMPs)

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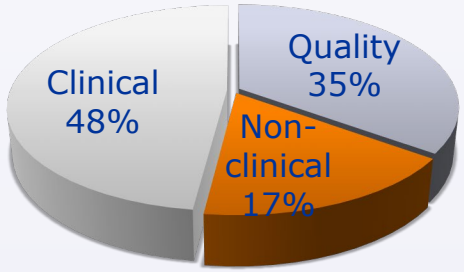
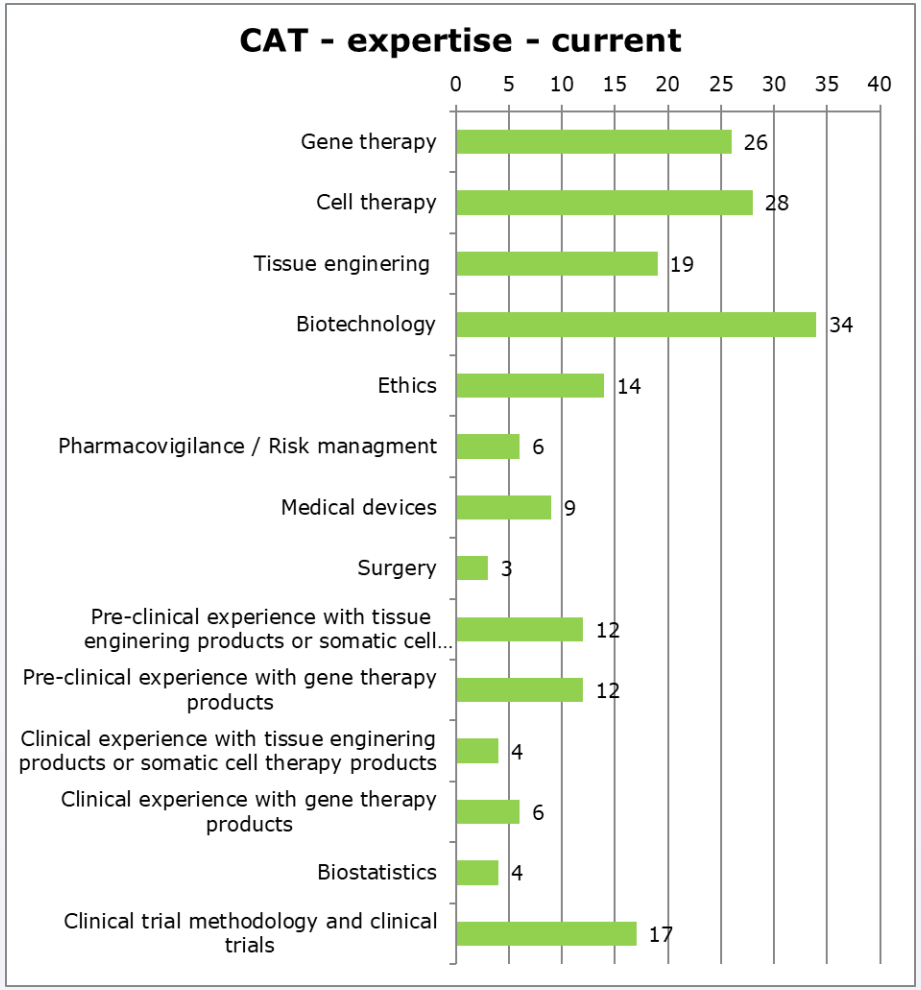
- In December 2008, the **ATMP Regulation (EC) No 1394/2007** entered into force laying down an **EU framework for marketing of Advanced Therapy Medicinal Products (ATMPs)**
- In 2009 the Committee for Advanced Therapies (CAT) was created **to provide expert regulatory and scientific advice specific to ATMPs**



- CAT: Multidisciplinary **scientific and regulatory expertise**




10.12.2007 EN Official Journal of the European Union L 324/121

REGULATION (EC) No 1394/2007 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 13 November 2007
on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004
(Text with EEA relevance)

https://www.ema.europa.eu/en/committees/committee-advanced-therapies-cat

CAT stands for

- Safe and efficacious first-in-class ATMPs
- Including incremental scientific-clinical knowledge in regulatory decision making
- Supporting ATMP developers
- Incorporating physician and patient perspectives in our deliverables
- Supporting patient access by analysing root causes of RWD deficiencies and by increasing interactions with HTAs
- Warning against unproven cell-based therapies
- Strengthened communication and exchange with EMA committees and working parties

What are the main differences to other medicines?

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- Complex products to develop, manufacture, characterise, test
- They do not follow standard non-clinical & clinical development programmes
- They bring novel toxicities, therefore they need risk assessment of insertional mutagenesis events
- Specific post-authorization obligations to address remaining uncertainties
- No precedent cases for regulatory decision making

Gene Therapy: two approaches to treat severe diseases

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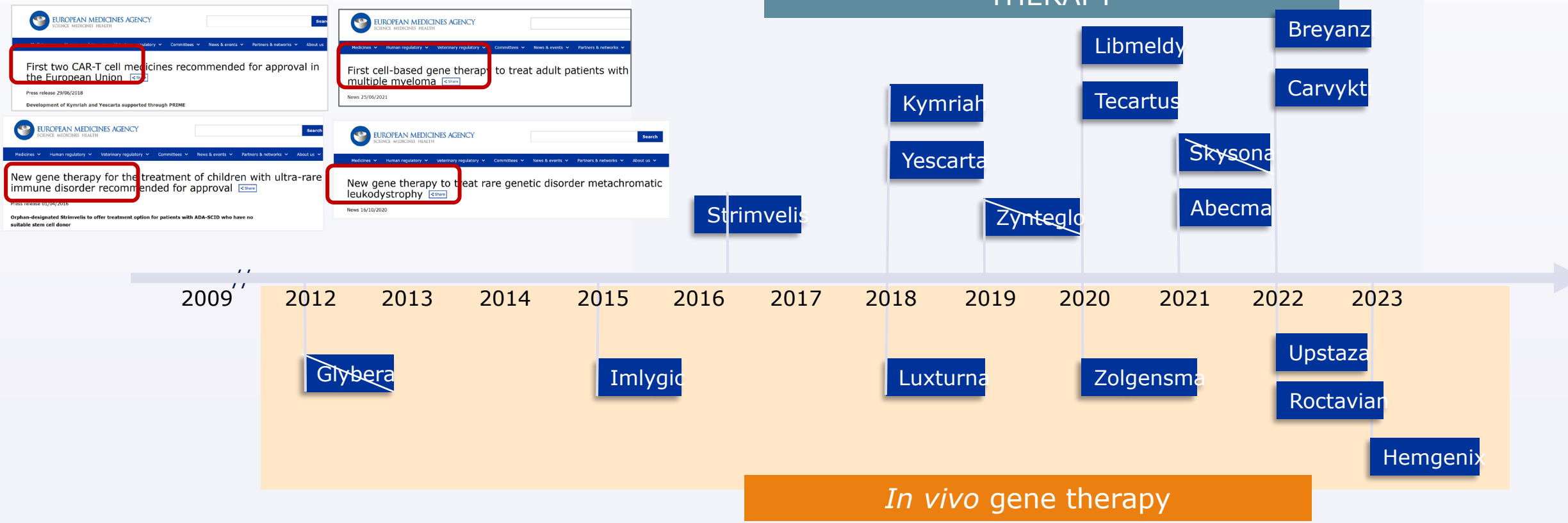

Innovative Somatic Cell Therapies Medicinal Products


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New medicine to treat perianal fistulas in patients with Crohn's disease

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Press release 15/12/2017

Alofisel is the tenth advanced therapy recommended for marketing authorisation


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First therapy to treat transplant patients with post-transplant lymphoproliferative disease

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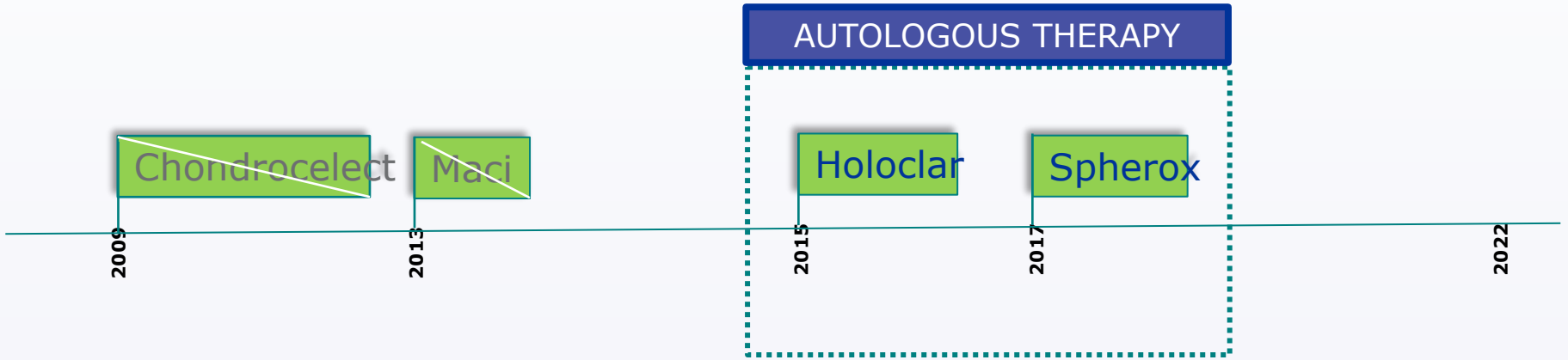
News 14/10/2022

- Provenge® Metastatic prostate cancer, 2013
- Zalmoxis® Stem cell transplantation, adjunctive treatment, 2016
- Alofisel® Crohn`s disease, complex anal fistula, 2017

- Ebvallo Tabelecleucel is an **allogeneic Epstein-Barr virus (EBV)-specific T-cell immunotherapy**

Innovative Tissue Engineered Medicinal Products

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First stem-cell therapy recommended for approval in EU

Press release 19/12/2014

New treatment for rare condition caused by burns to the eye

The European Medicines Agency (EMA) has recommended Holoclar, the first advanced therapy medicinal product (ATMP) containing stem cells, for approval in the European Union (EU). Holoclar is a treatment for


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New advanced therapy to repair cartilage defects in the knee

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Press release 19/05/2017

Spherox recommended for marketing authorisation

- Chondrocelect® Cultured chondrocytes for repair of knee cartilage defects, 2009
- MACI® Cultured chondrocytes…..2013
- Spherox® Cultured chondrocytes……2017
- Holoclar® Cultured corneal epithelial cells for treatment of corneal lesions 2014

HEMGENIX (INN-etranacogene dezaparvovec)

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- Treatment of Haemophilia B for adults with congenital Factor IX definciency.
- Non-replicating, recombinant adeno-associated virus serotype 5 (AAV5) based vector.
- Single dose, intravenous (after at least 6 months with standard routine Factor IX prophylaxis)
- 2 prospective, open-label, single-dose, single-arm studies.
  - ✓ Phase 2b study performed in US (N=3)
  - ✓ Phase 3 multi-national study performed in US, UK and EU (N=54)
  - ✓ Adult male patients with moderately severe or severe Haemophilia B
  - ✓ 5 years follow-up

HEMGENIX (INN-etranacogene dezaparvovec) (II)

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- Study results: primary endpoint: assessment of the annualised bleeding rate compared to the observational lead-in period:

Number	≥6-month lead-in period FAS (N=54)	7-18 months post-dose FAS (N=54)	≥6-month lead-in period (N=53)***	7-18 months post-dose (N=53)***
Number of patients with bleeds	40 (74.1%)	20 (37.0%)	40 (75.5%)	19 (35.8%)
Number of patients with zero bleeds	14 (25.9%)	34 (63.0%)	13 (24.5%)	34 (64.2%)
Number of any bleeds	136	54	136	49
Number of person years for bleeding events	33.12	49.78		
Adjusted* ABR** (95% CI) for any bleeds	4.19 (3.22, 5.45)	1.51 (0.81, 2.82)	3.89 (2.93, 5.16)	1.07 (0.63, 1.82)
ABR reduction (lead-in to post-treatment) 2-sided 95% Wald CI 1-sided p-value****	-	64% (36%, 80%) 0.0002		72% (57%, 83%) p<0.0001

HEMGENIX (INN-etranacogene dezaparvovec)

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- Conditional aproval February 2023.
- Post MA Long-term follow up: 15 years
- Registry based study: 31/Dec/2044

Highlights 2023

- Improve interactions with HTAs
- Gain knowledge on the possibilities of RWD/RWE for regulatory decision making
- Interactions with stakeholders:
  - ✓ Learned societies
  - ✓ Industry
  - ✓ Regulators (FDA, Japan)
- Progress on the Guideline on requirements for investigational ATMPs in clinical trials
- Post -authorisation safety and efficacy follow-up and RMP for ATMPs

CAT’s added value

- First in class first in human
- Urgent unmet medical needs & limited evidence
- Deliberation & apropriation by all the committee
- Use of RWD/RWE for regulatory decisions (pre & post MA)

Many thanks!
Any questions?

Acknowledgements:

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