Exploring the Evolution of the Biotherapies Revolution

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Disclosures

- No relevant financial disclosures
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- Member of apheresis working group in the NHLBI Cure Sickle Cell Initiative

Learning objectives

By the end of this presentation, audience members should be able to:

- Describe general characteristics of biotherapies in clinical use
- Compare biotherapies under development in anticipation of clinical use

Defining biotherapies

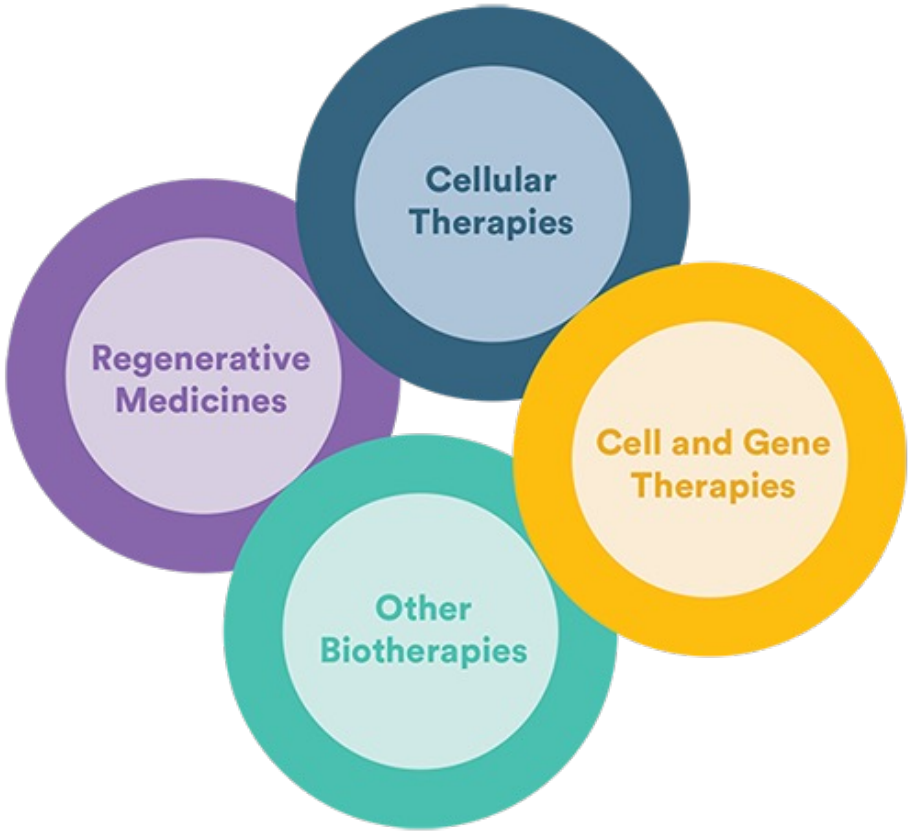
- Substances made from living organisms to treat disease that may occur naturally in the body or may be made in the laboratory

- Types of biotherapy can include (a few examples):

  - Molecules
    - cytokines
    - cancer vaccines
    - Antibodies

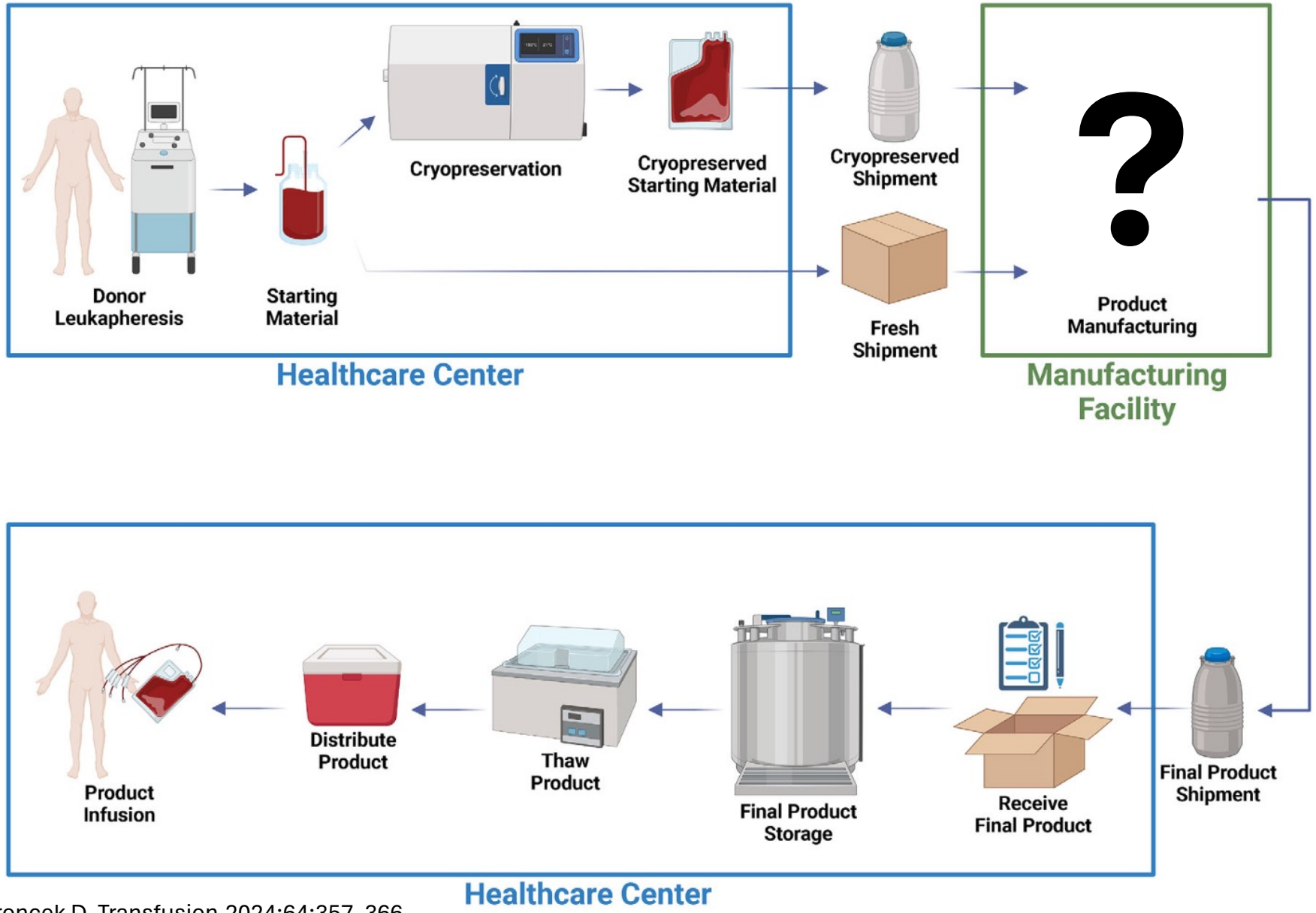
  - Cells
    - Blood transfusions (the original biotherapy!)
    - hematopoeitic stem cell transplants

  - Genetically modified cells
    - Chimeric antigen receptor T cells
    - Genetically modified hematopoietic stem cells



https://www.cancer.gov/publications/dictionaries/cancer-terms/def/biotherapy, https://www.aabb.org/news-resources/resources/cellular-therapies

Manufacturing genetically modified cells is a complex process



Adapted from: Dinh A and Stroncek D. Transfusion.2024;64:357–366

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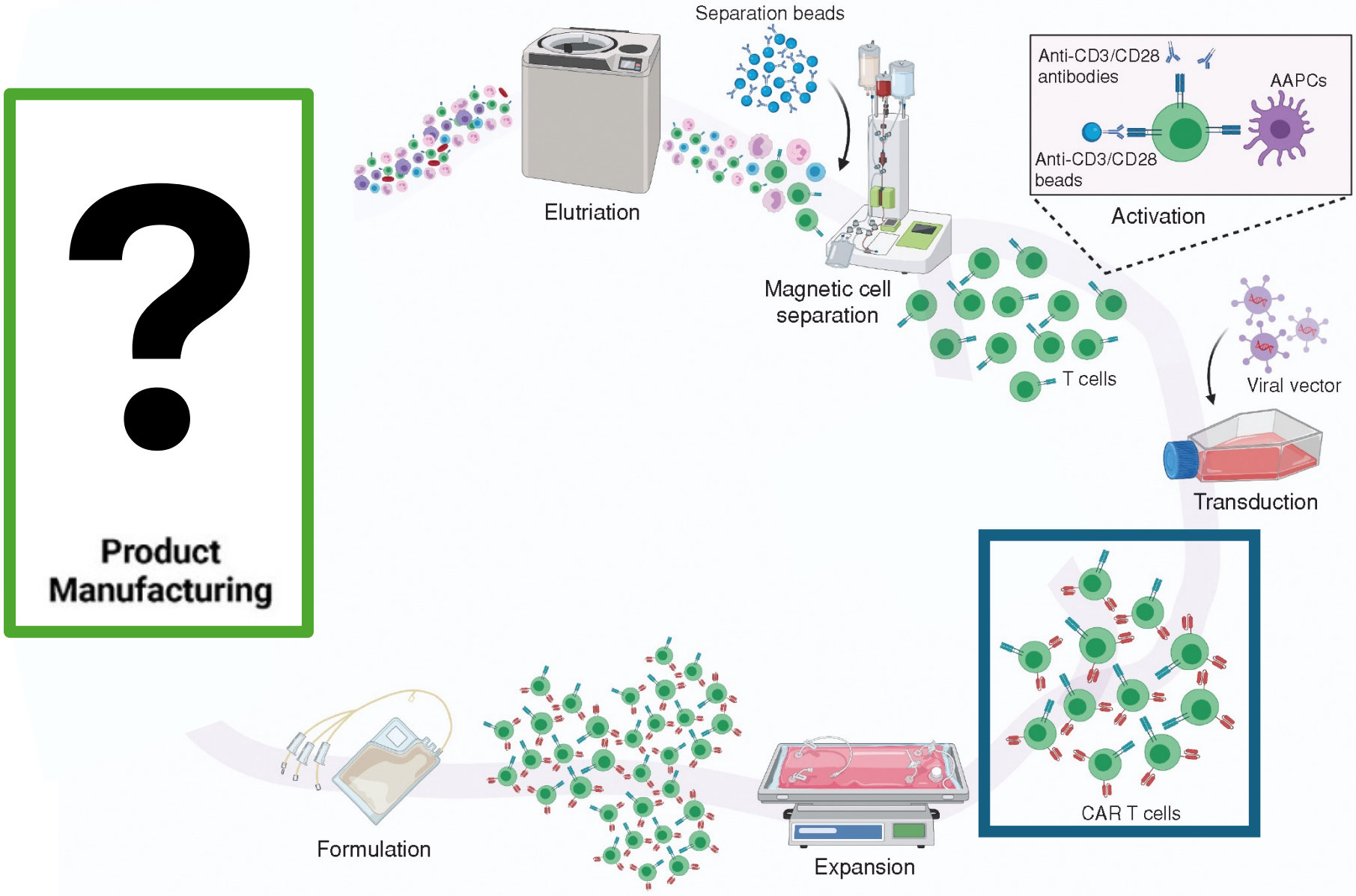
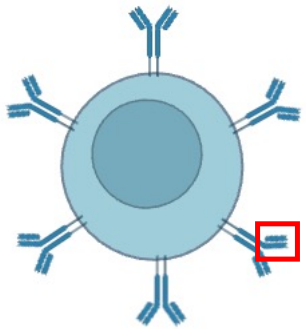


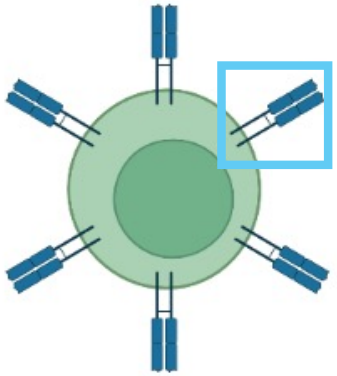
Adapted from: Blood Cancer Discov. 2021;2(5):408-422. doi:10.1158/2643-3230.BCD-21-0084

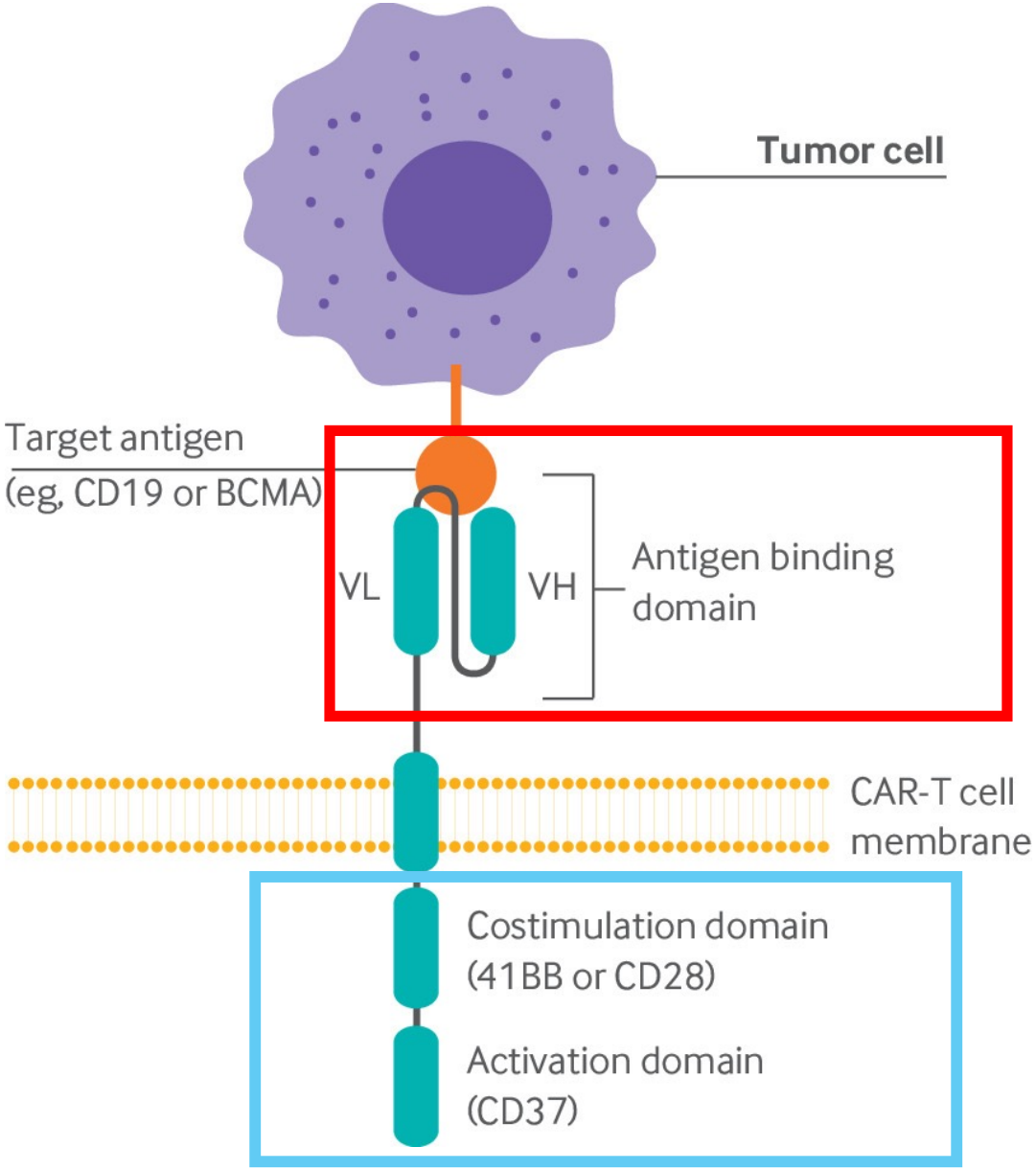
Chimeric Antigen Receptor (CAR) T cells combines the best of B cell and T cell functions



B cell (with antibodies)

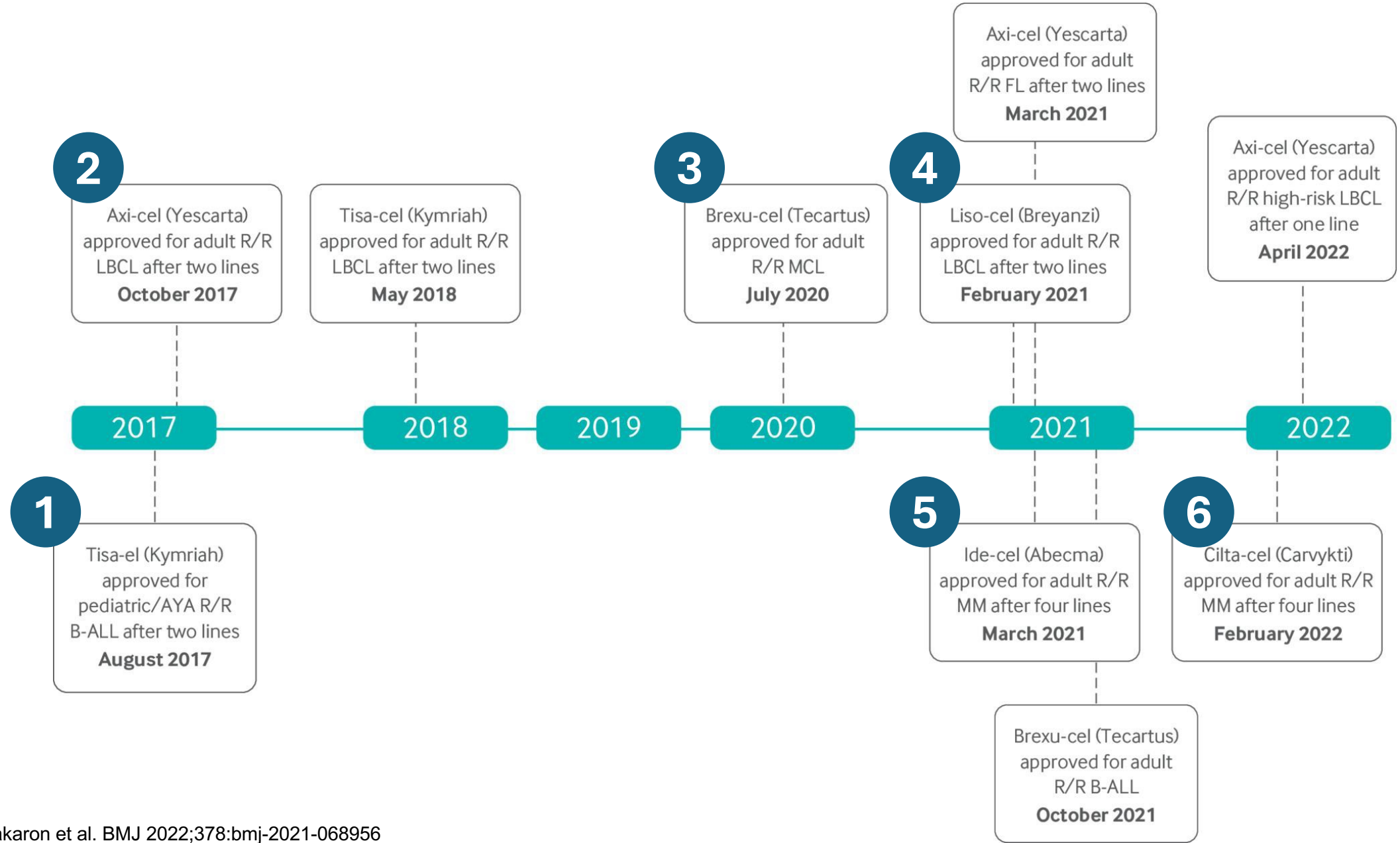
T-cell (with TCRs)





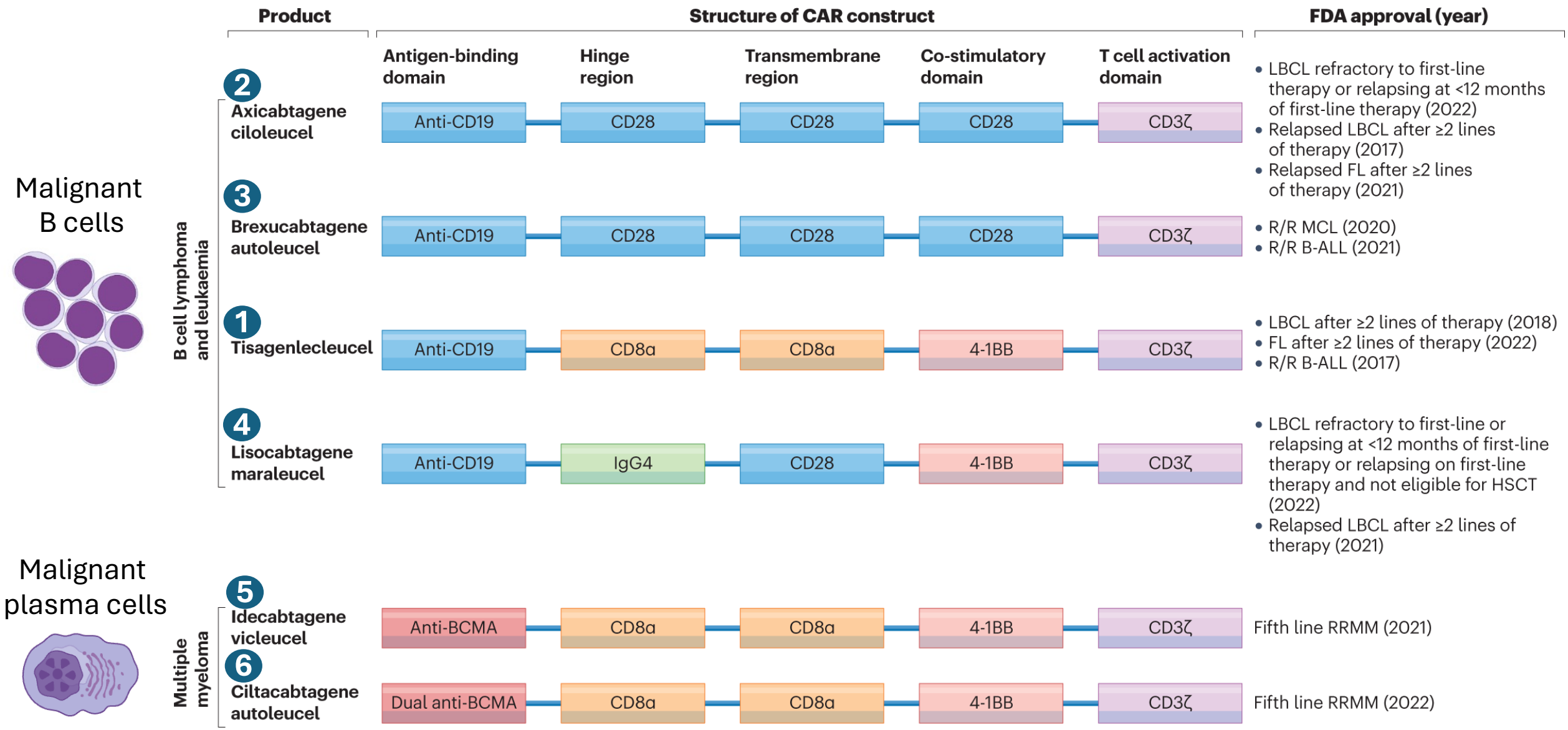
BMJ 2022;378:e068956

There are currently 6 CAR T cells approved for clinical use



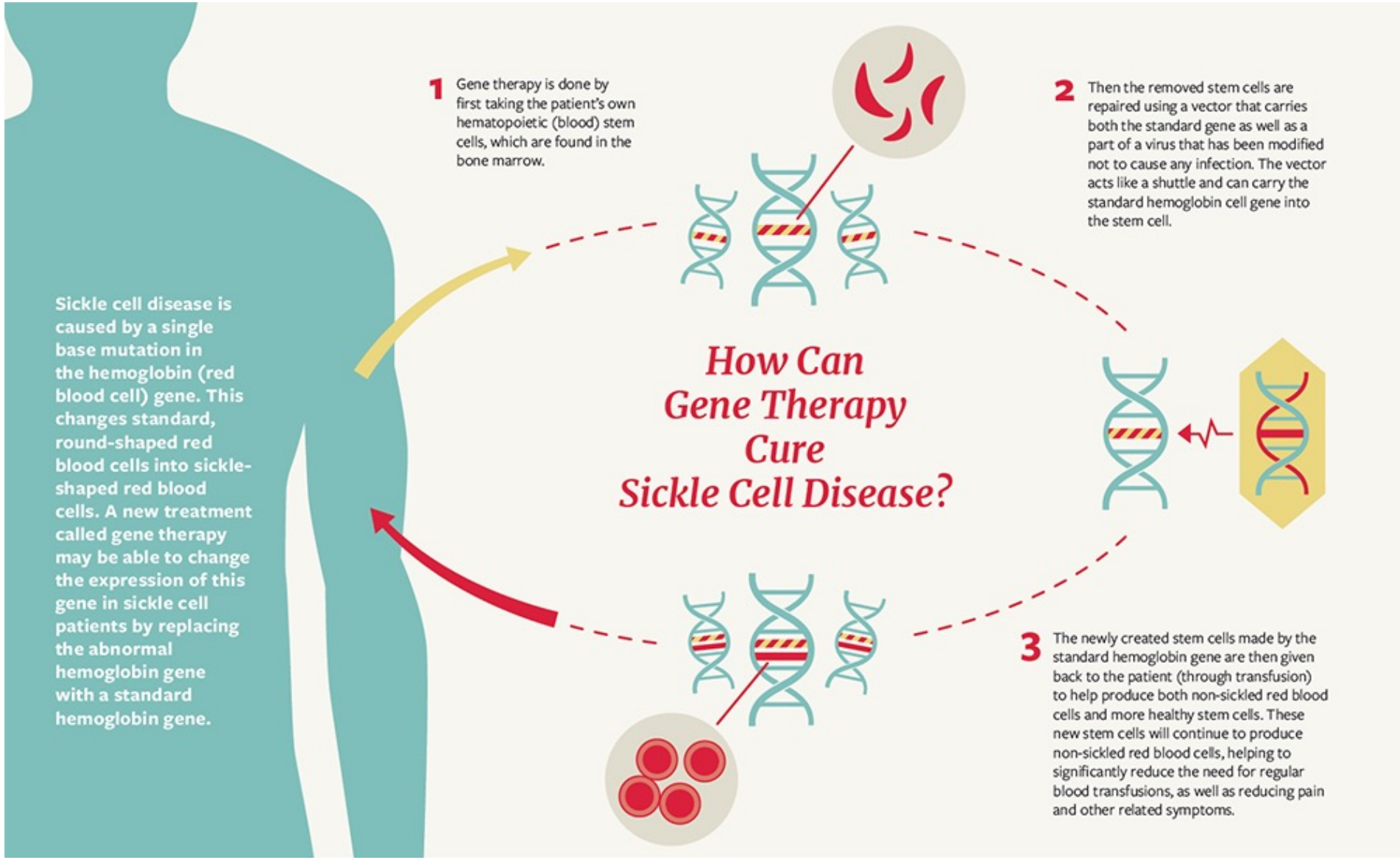
Joseph E Maakaron et al. BMJ 2022;378:bmj-2021-068956

Each approved CAR T cell has unique attributes



Cappell, K.M., Kochenderfer, J.N. *Nat Rev Clin Oncol* **20**, 359–371 (2023)

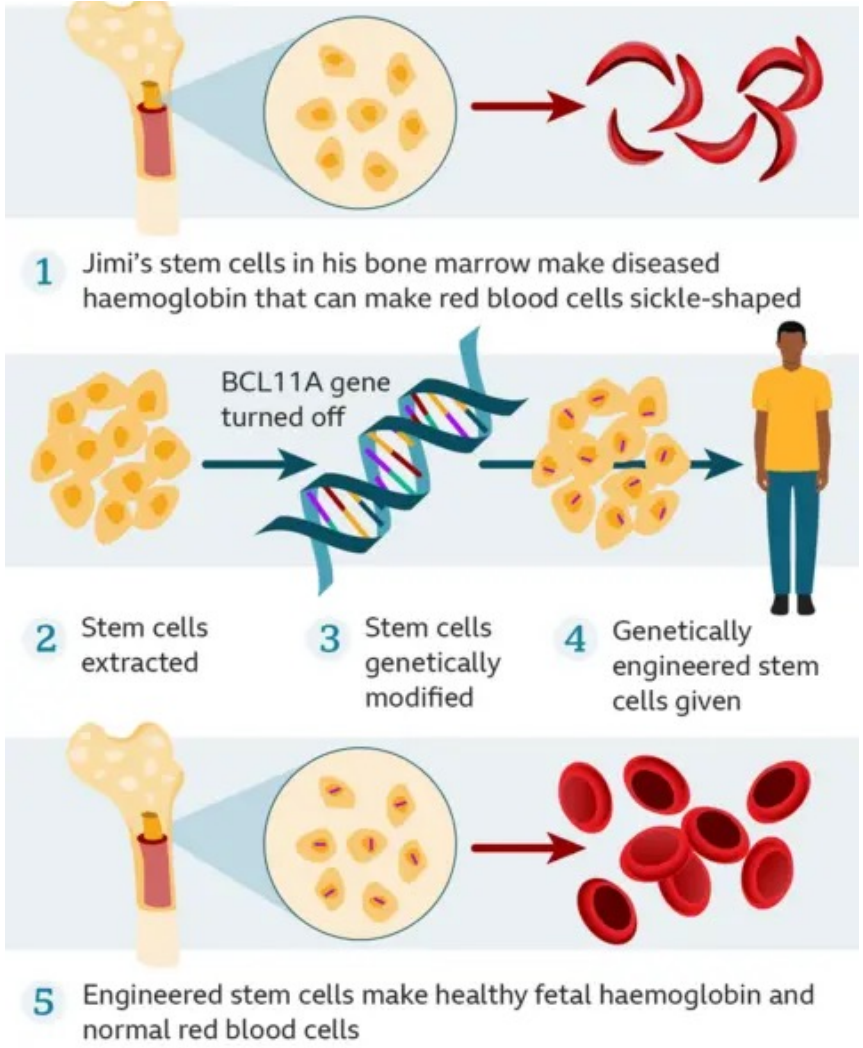
Not just CARs anymore: genetically modified hematopoietic stem cells were recently approved



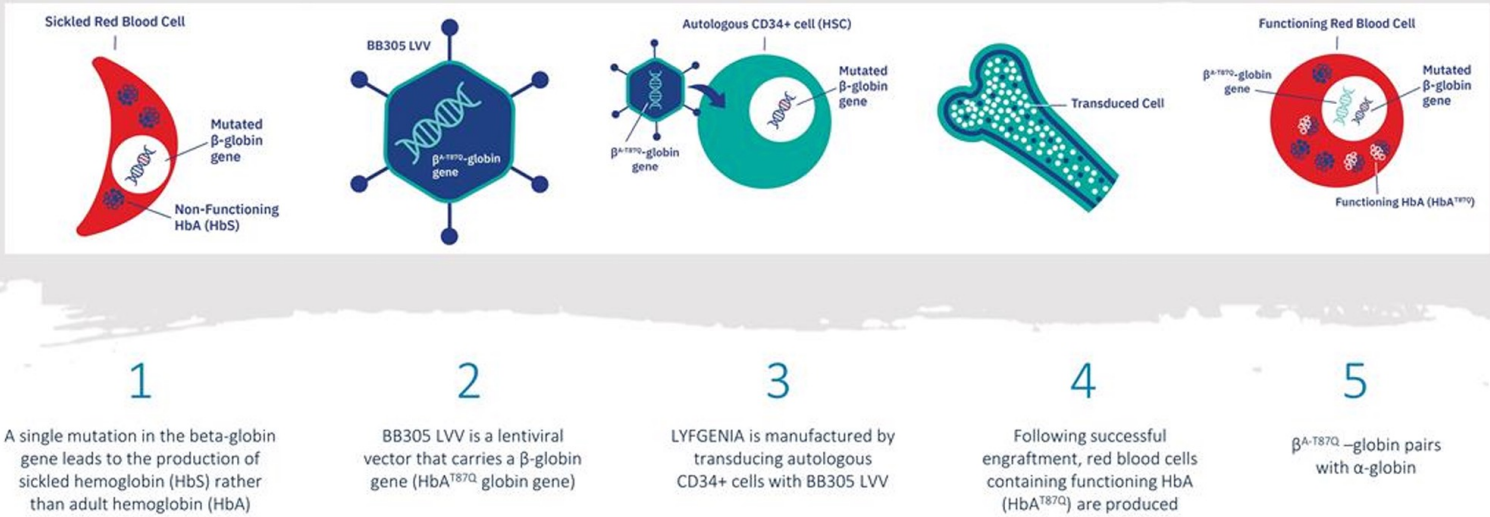
https://curesickle.org/sites/scdc/themes/scdc/images/CSC_GenetherapyInfographicSELF.png

Each approved genetically modified hematopoietic stem cell has unique attributes

exagamglogene autotemcel (exa-cel)

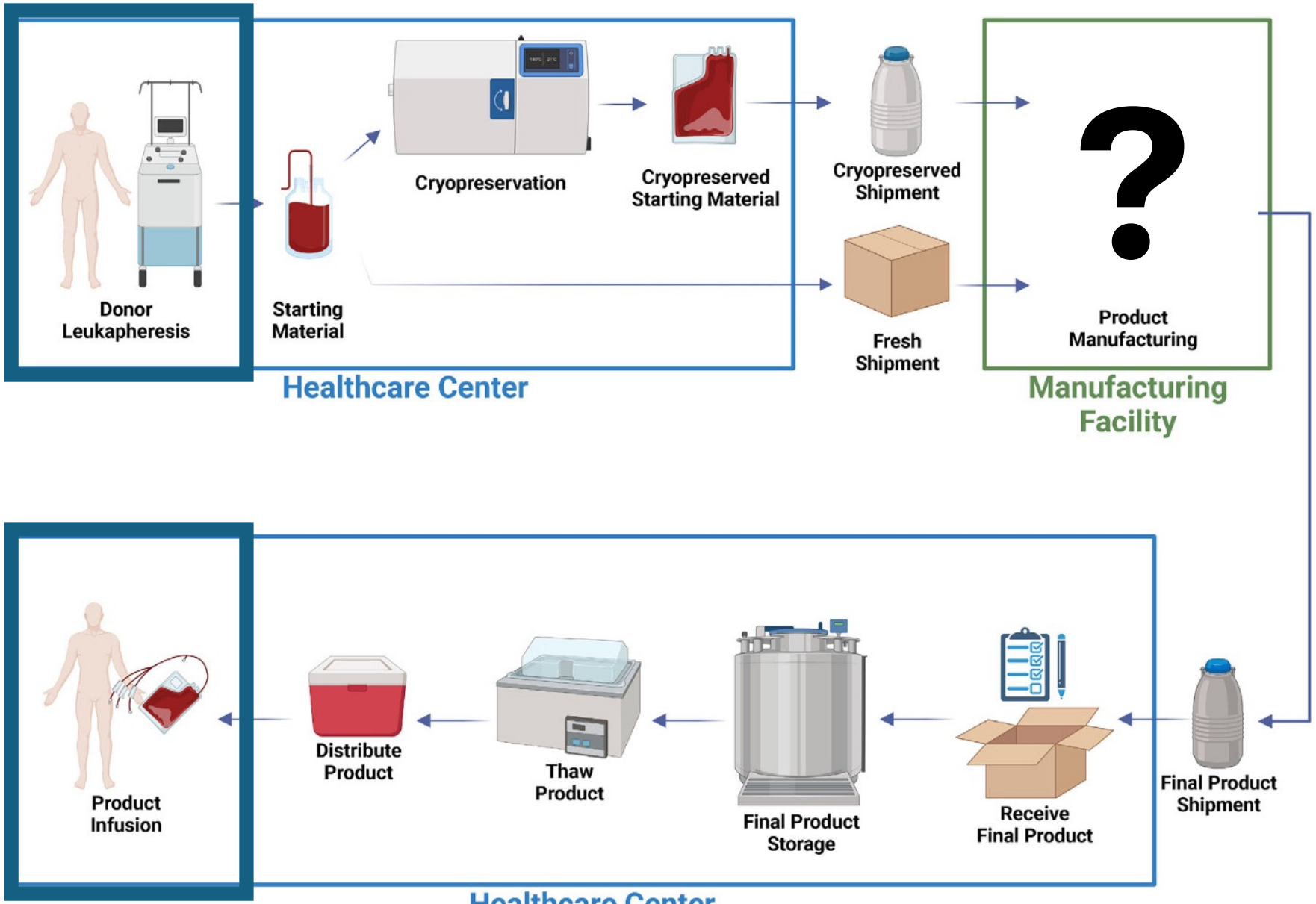


lovotibeglogene autotemcel (lovo-cel)



https://www.bbc.com/news/health-67435266, https://investor.bluebirdbio.com/static-files/1953f998-cf49-4cfb-8e88-d52c0a9b7528

The future of cell and gene therapies is wide open



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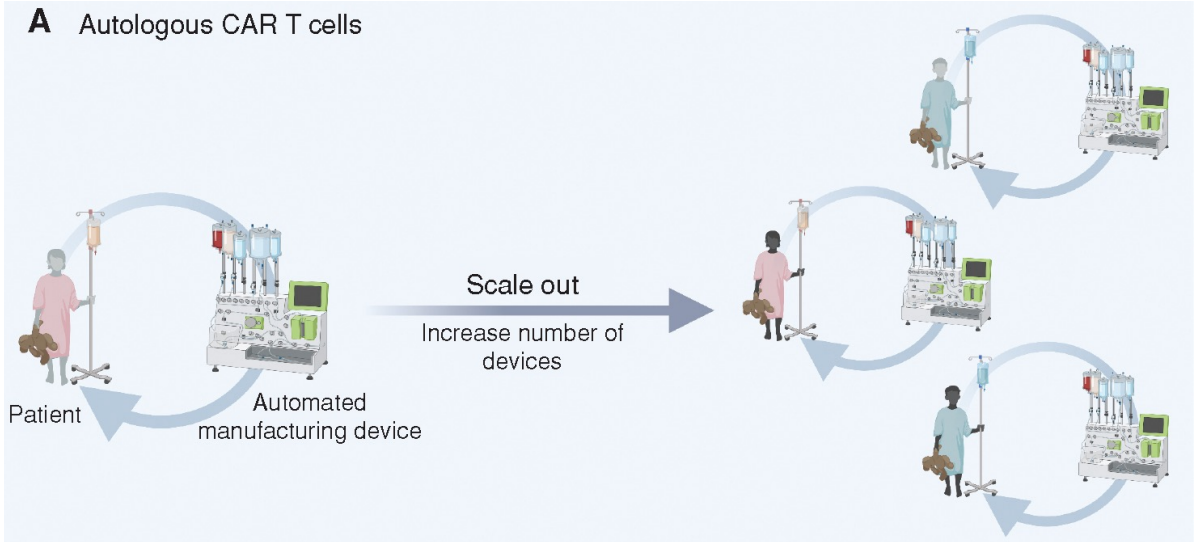
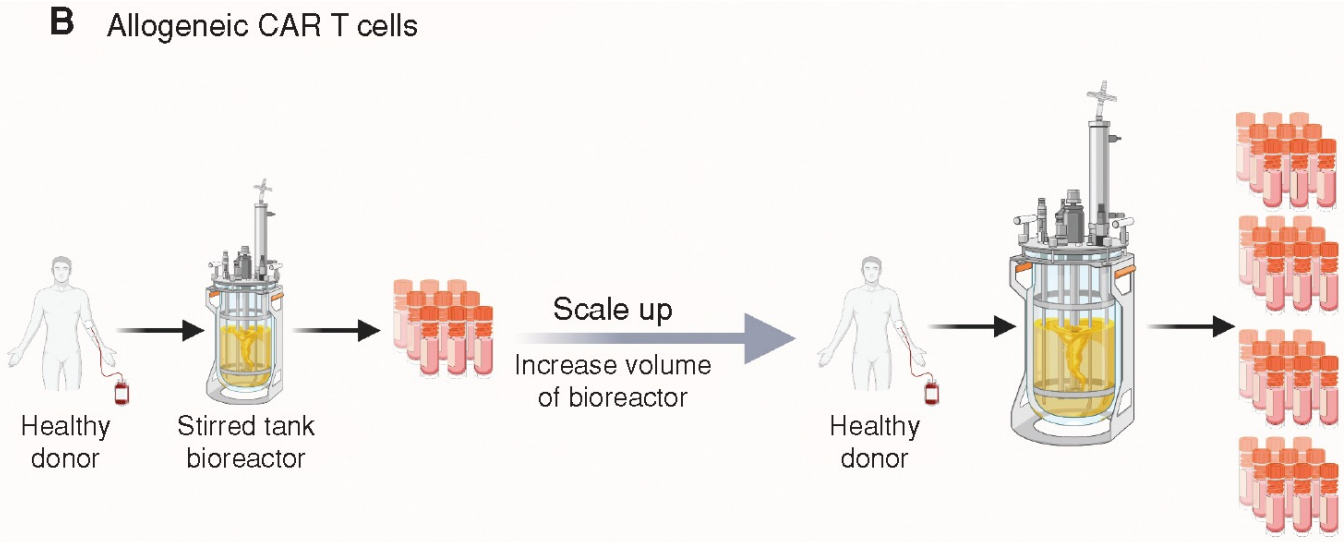
Current state

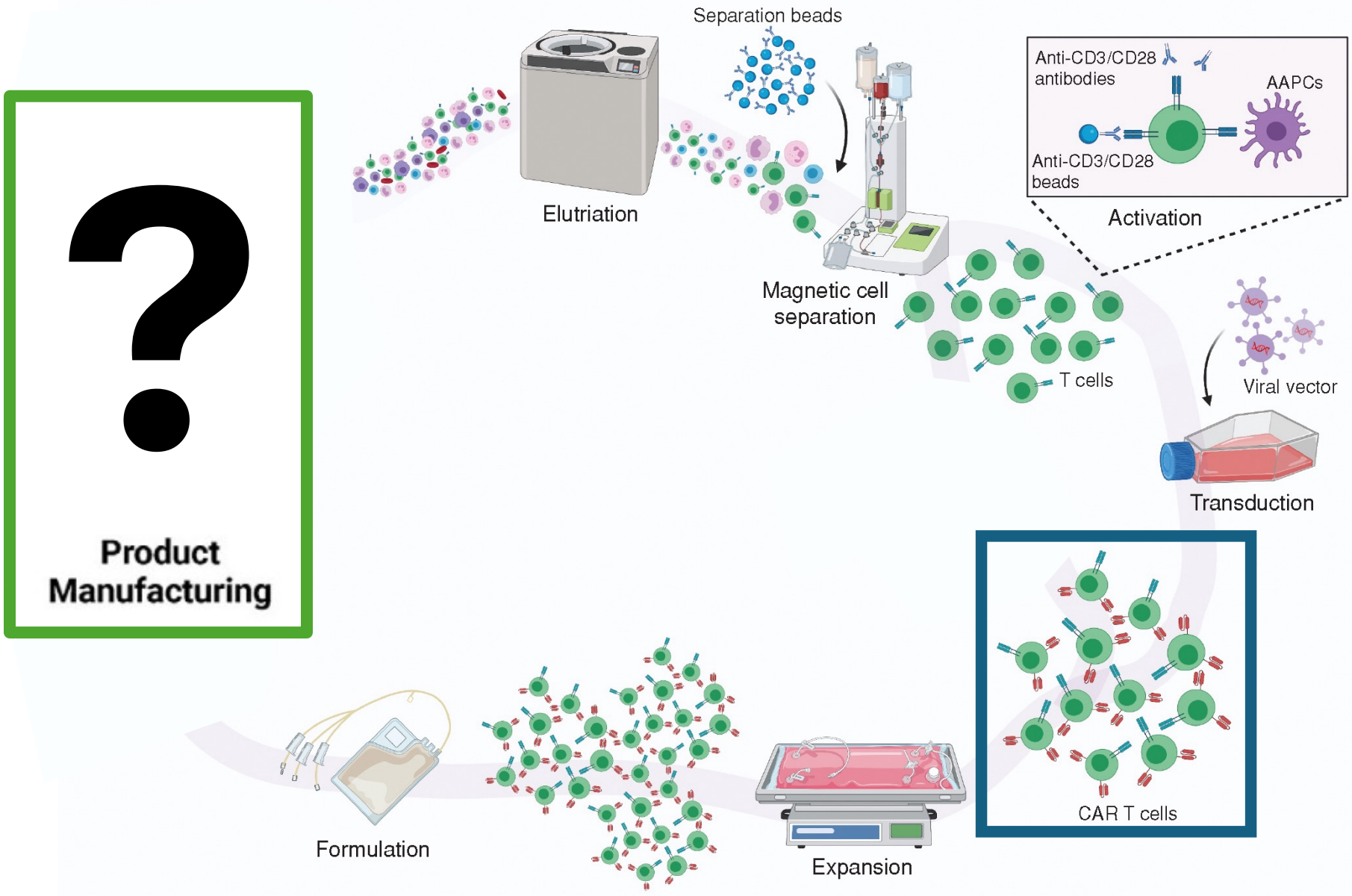


Future state?



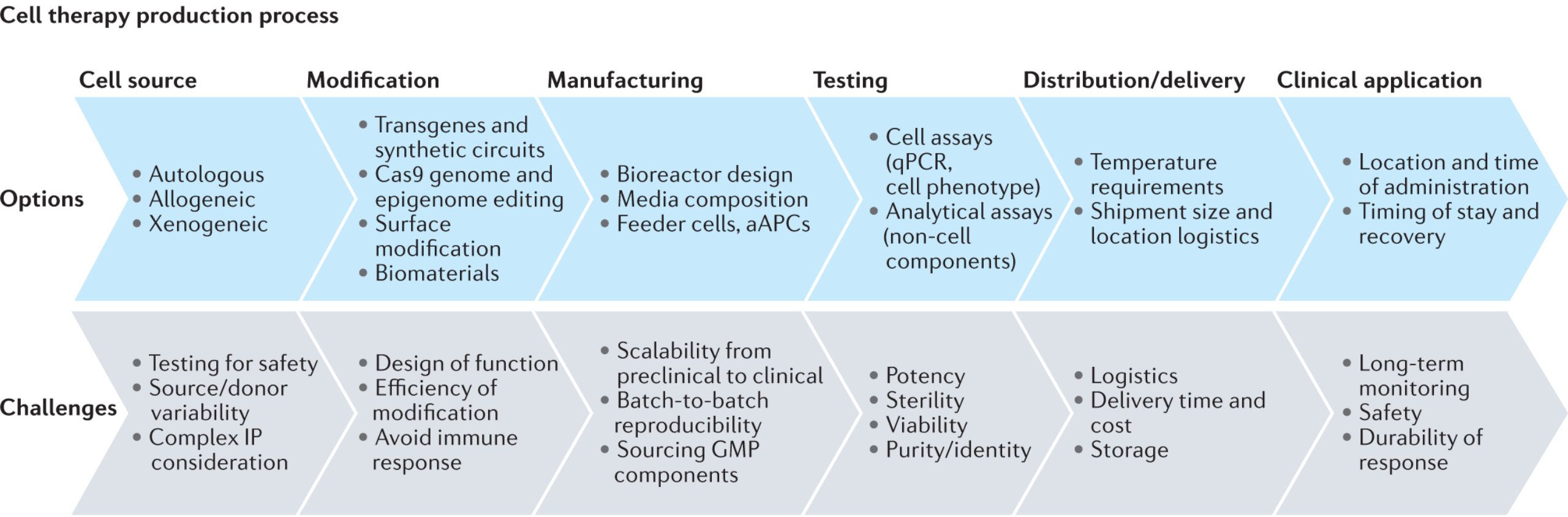
Blood Cancer Discov. 2021;2(5):408-422. doi:10.1158/2643-3230.BCD-21-0084

Any substantial change in the process = a new product



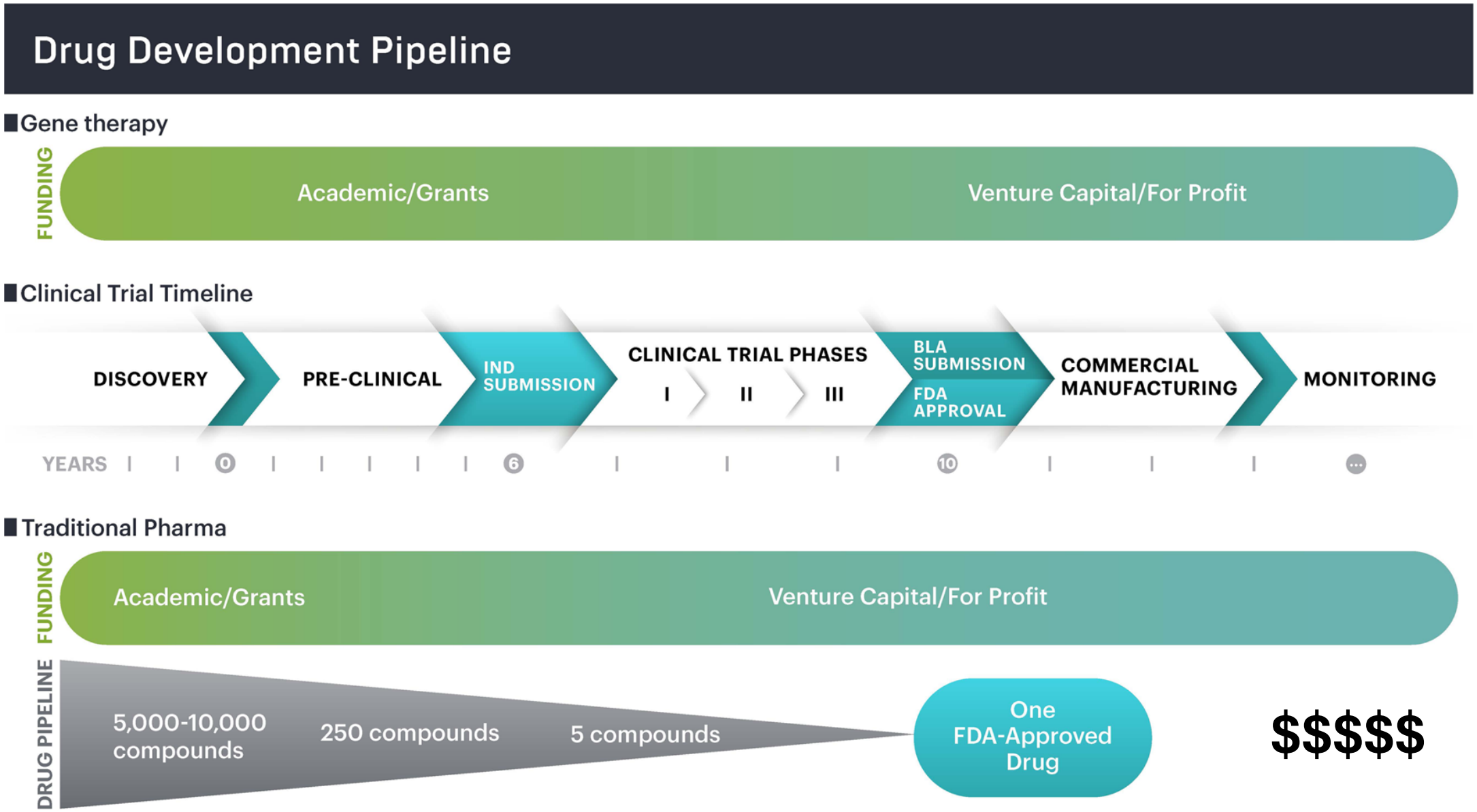
Adapted from: Blood Cancer Discov. 2021;2(5):408-422. doi:10.1158/2643-3230.BCD-21-0084

New products must be fully vetted at every stage of the process



Bashor, C.J., *et al*. *Nat Rev Drug Discov* **21**, 655–675 (2022)

New products can take decades to reach approval



Witkowsky, *et al.* *Gene Ther* **30**, 747–752 (2023)

No treatment is without risk

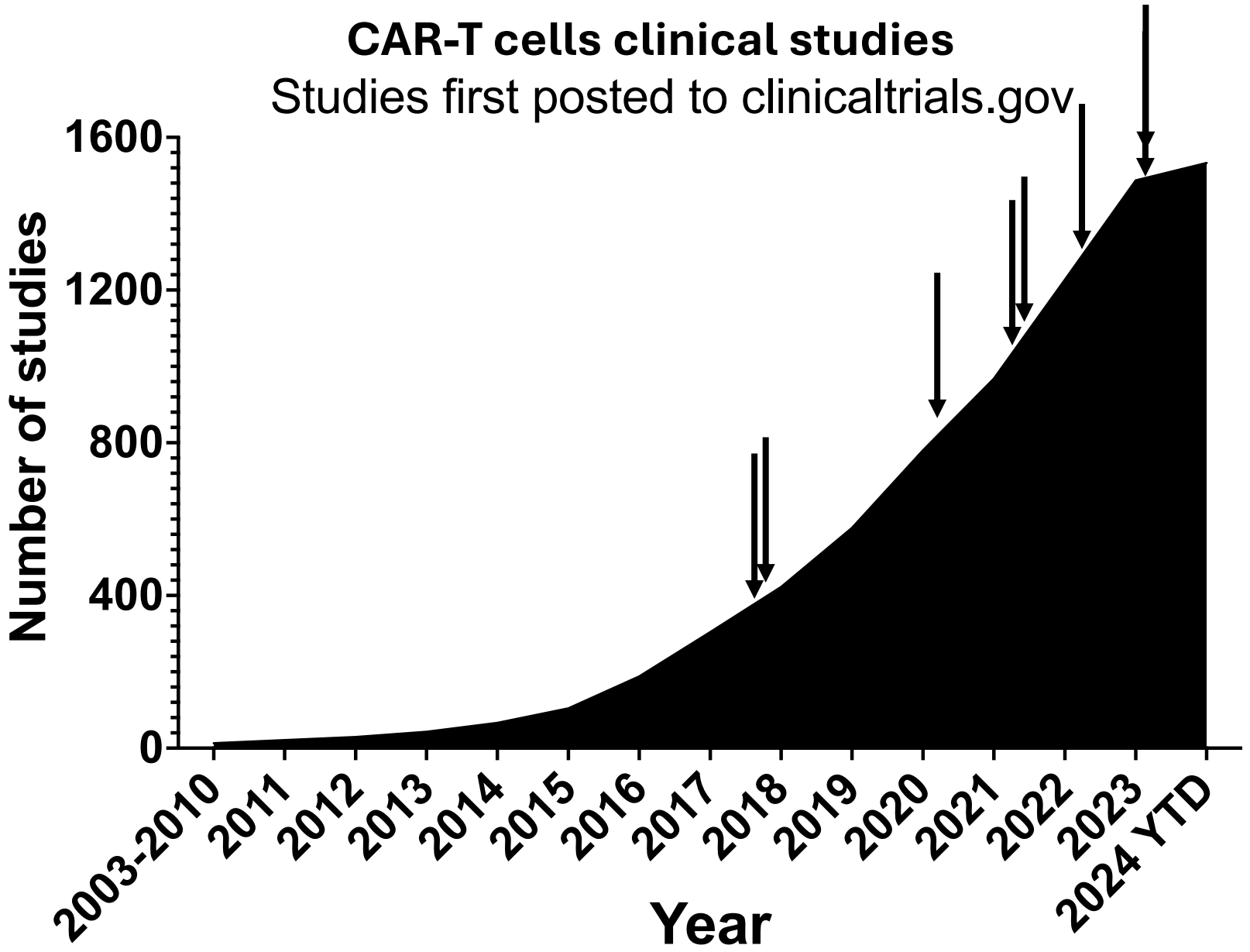
WARNING: HEMATOLOGIC MALIGNANCY
See full prescribing information for complete boxed warning.

Hematologic malignancy has occurred in patients treated with Monitor patients closely for evidence of malignancy through complete blood counts at least every 6 months and through integration site analysis at Months 6, 12, and as warranted. (5.1)

4/18/24

FDA Requires Boxed Warning for T cell Malignancies Following Treatment with BCMA-Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T cell Immunotherapies

Cellular therapies under clinical development is exploding



Clinicaltrials.gov, search for “chimeric antigen receptor T cells”, accessed February 2024.

Conclusions and considerations

- Genetically modified biotherapies in clinical use include:
  - CAR T cells for B cell malignancies
  - CAR T cells for multiple myeloma
  - Genetically modified hematopoietic stem cells for hemoglobinopathies

- Many parts of the process are under study for new products
  - Source of cells
  - Target
  - disease indication
  - Manufacturing process
  - Etc.

It is an exciting time to be in the field of biotherapies!

Thank you!