



The Way Ahead for Cell and Gene Therapies: How to Create Healthcare System Infrastructure that Supports New Pathways to Access and Reimbursement

Canadian Institute 9th Annual Forum: Pathways To Access & Reimbursement
February 13, 2024, 11:30am



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Access Solutions

Talk synopsis

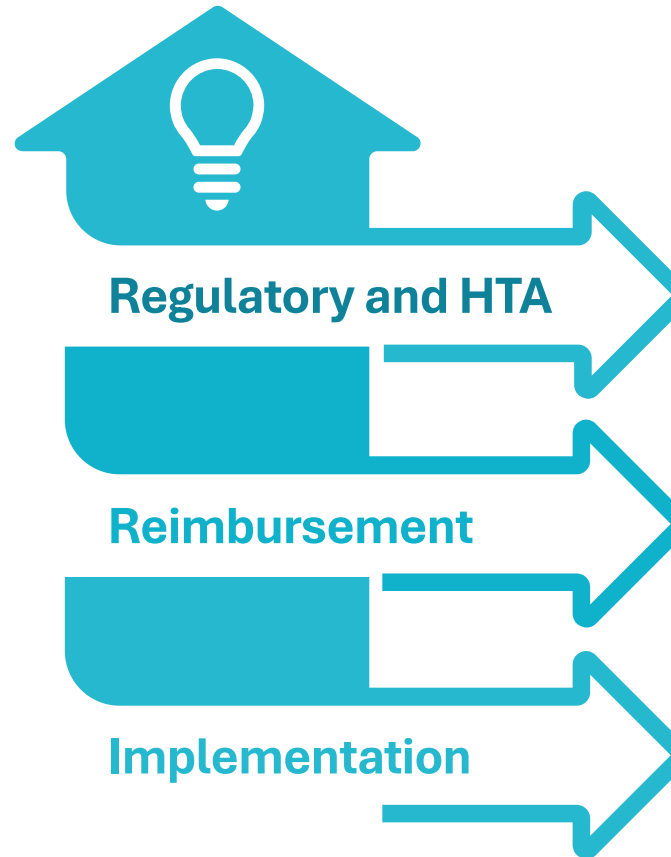
**Life-changing
Innovative**



Life-saving

**High-cost
Rare Disease**

Million-dollar



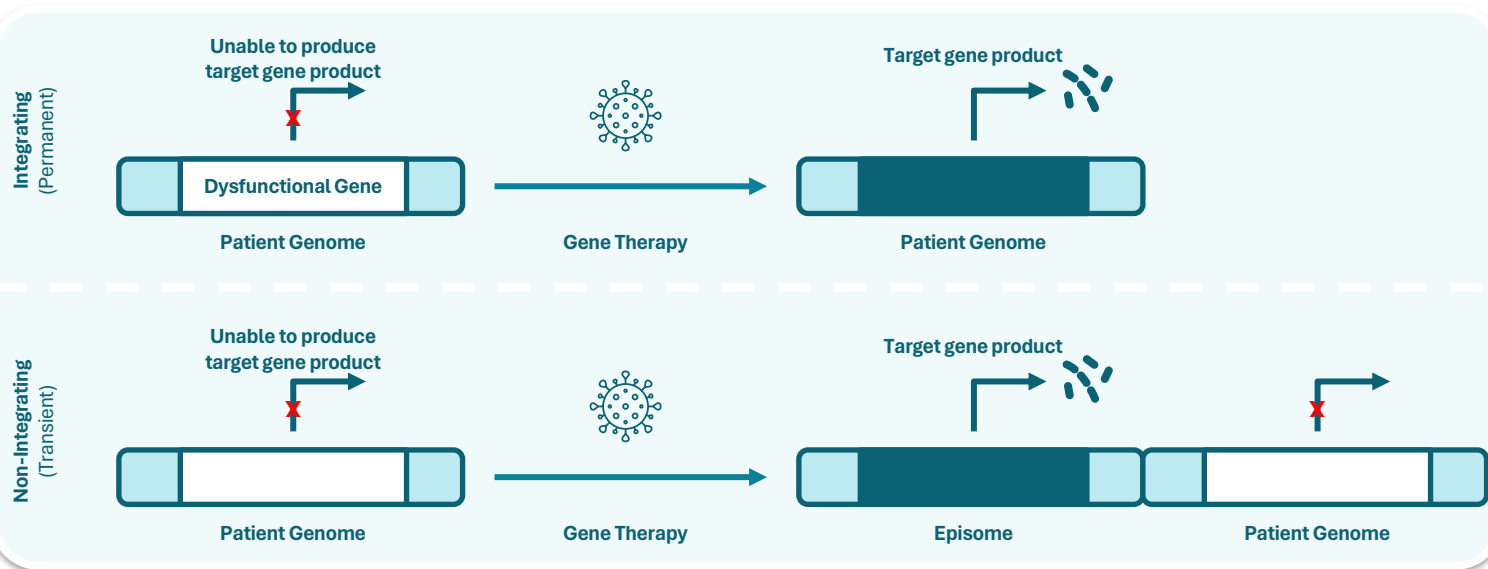
Navigating Canada's regulatory and HTA pathways for cell and gene therapy

Gaps in reimbursement and infrastructure for complex gene therapies

Obstacles to adoption, implementation, and financing



The different technologies involved in cell and gene therapy

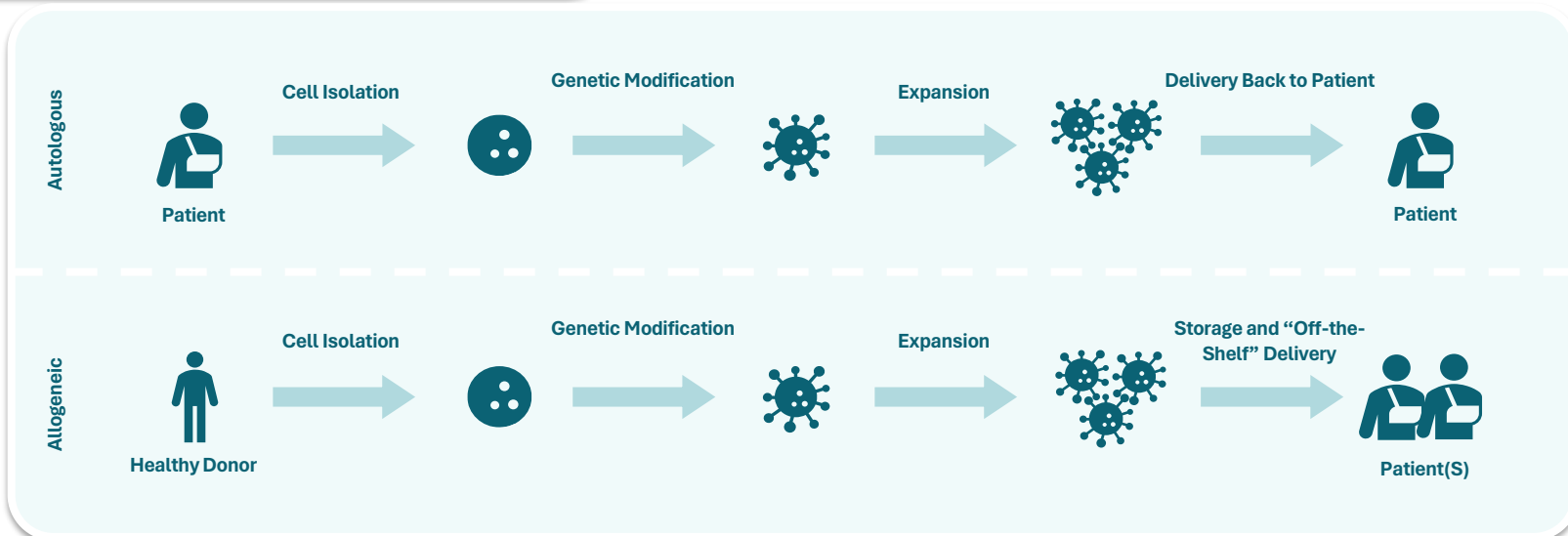


GENE THERAPY

Gene therapies treat genetic diseases by replacing dysfunctional genes. Genetic information is delivered to patients using “vectors,” such as adeno-associated viruses (AAVs), lentiviruses, liposomes, and beyond.

CELL THERAPY

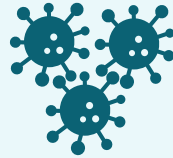
Cell therapies treat diseases with living cells isolated from humans. These cells are commonly modified to increase target recognition and activity.



Four main types of cell and gene therapies in late-stage development

Genetically modified cell-based immunotherapies

- ❖ CAR-T cell therapies
- ❖ TCR therapies
- ❖ NK cell therapies



Viral vectors

- ❖ Adeno-associated viruses (AAVs)
- ❖ Adenovirus
- ❖ Lentivirus



Gene editing

- ❖ CRISPR/Cas
- ❖ Homologous recombination of AAV-derived sequences



Non-viral vectors

- ❖ Nanoparticles
- ❖ Nanospheres



Cell and gene therapies present unique opportunities and challenges to the healthcare system



Cell & Gene Therapy

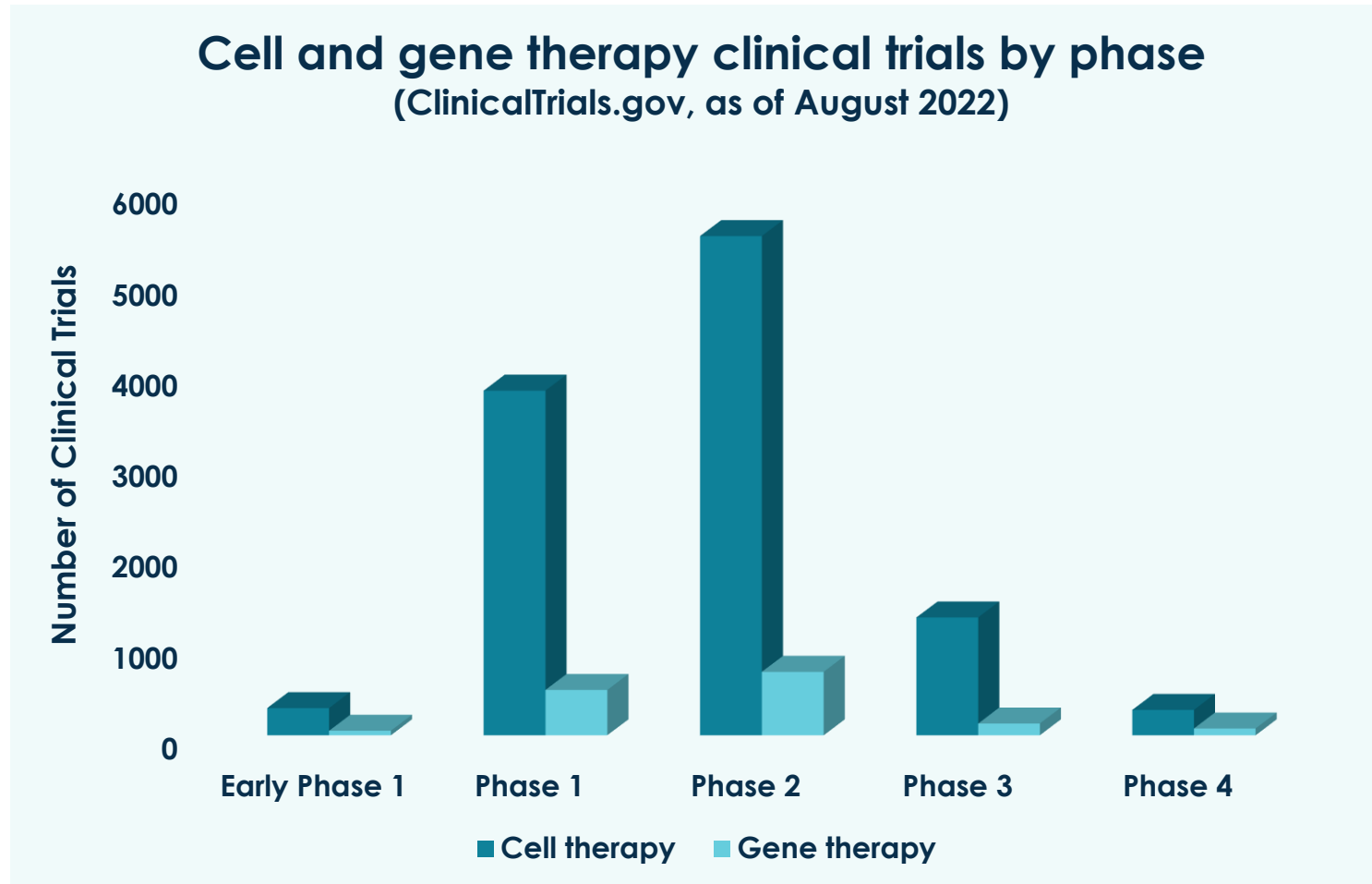


Traditional Therapy

One-time, curative intent		Treatment Course/ Benefit	Longer term, continuous disease management
Expensive and complex, sometimes individualized, not easily scalable		Manufacturing	Traditional manufacturing and supply chain
\$\$\$		Cost	\$
Unique, more complex infrastructure and distribution		Implementation	Well-known implementation and distribution
Limited		Clinical Expertise	Well established
Less experience, more uncertainty		Patient Experience	More experience, more trust
Unclear post-patent pathway		Product Life Cycle	Genericization and biosimilar entry after patent expiration

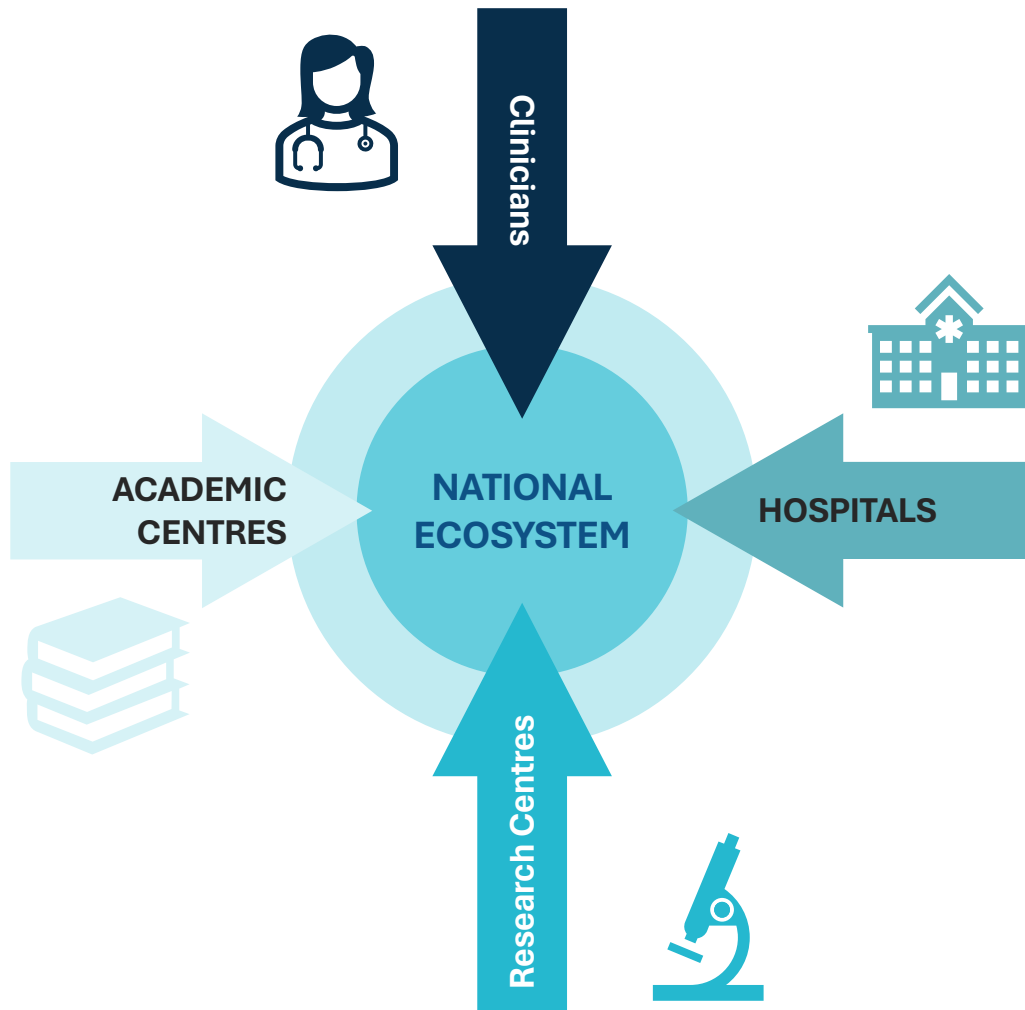


Large numbers of cell & gene therapies are in development



Source: Lee, SungKyung, and Jong Hyuk Lee. "Cell and gene therapy regulatory, pricing, and reimbursement framework: With a focus on South Korea and the EU." *Frontiers in Public Health* 11 (2023): 1109873.

Canada is interested in building a national ecosystem for health innovation in the area of cell and gene therapies



The National Research Council (NRC) Canada's **Disruptive Technology Solutions for Cell and Gene Therapy Challenge program**, in collaboration with academic facilities, research centres and hospitals, will aim to design and develop disruptive technology solutions for cell and gene therapies for the treatment/potential cure of chronic and rare diseases at a national level.





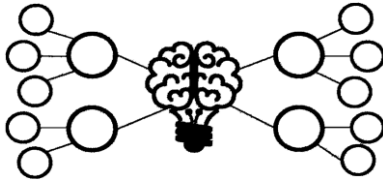
Regulatory and HTA



Managing regulatory challenges for cell and gene therapies

Challenges

Real Novelty & Complexity



- Rapidly evolving technology
- Complex mechanism of action
- Patient + product heterogeneity

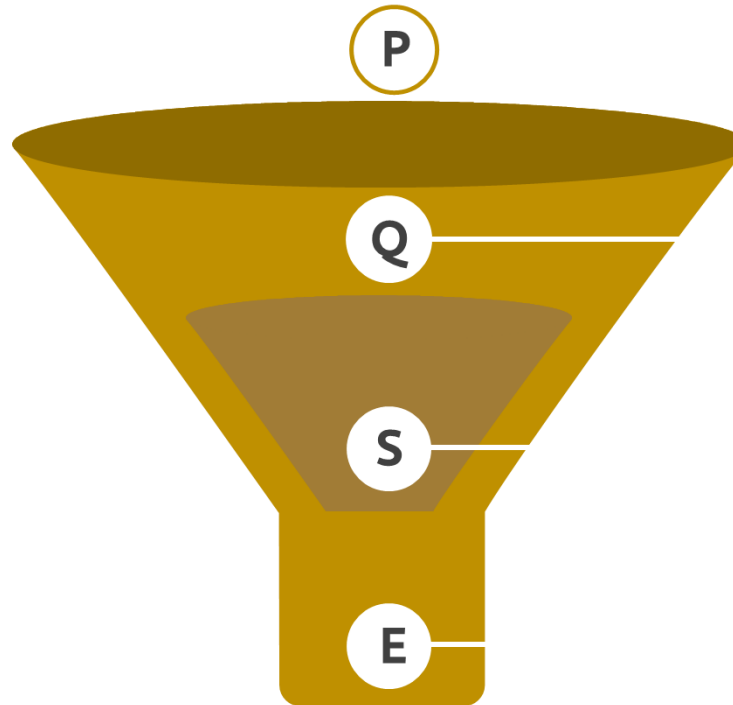
Perceived

“Regulatory Uncertainty”



- Limited guidance
- Unclear requirements
- Additional time & cost

Solutions



Plan to Quality by Design (QbD)

YOU tell regulators how your manufacturing, preclinical, and clinical development are aligned



Quality to Good Manufacturing Practices (GMP)

YOU tell regulators how you manufacture consistent products under “sanitary conditions”



Safety to Good Laboratory Practices (GLP)

YOU tell regulators how your materials and preclinical models are relevant



Efficacy to Good Clinical Practices (GCP)

YOU tell regulators how benefits are likely to outweigh risks in patients



Pfizer's Beqvez received NOC and positive CADTH draft recommendation even before FDA or EMA approval

CANADA IS CURRENTLY A FAVORABLE MARKET FOR CELL & GENE THERAPIES



FIDANACOGENE ELAPARVOVEC

(Beqvez)

- AAV vector-based gene therapy
- Indicated for treatment of adults with moderate to severe hemophilia B who are negative for neutralizing antibodies to variant AAV serotype Rh74r
- **Received regulatory approval in Canada earlier than USA & EU**

However, many cell & gene therapies have not launched in Canada



Cell and gene therapies have received favourable HTA recommendations from both CADTH and INESSS

Historical Cell & Gene Therapy CADTH Recommendations & List Prices in Canada

DRUG	COST	Indication	CADTH RECOMMENDATION	INESSS RECOMMENDATION
Abecma	\$545,000	Multiple Myeloma	Do not reimburse*	Do not reimburse*
Breyanzi	\$501,900	Relapsed or refractory large B-cell lymphoma	Recommend	Recommend
Zolgensma	\$2,910,500	Spinal muscular atrophy (SMA), pediatrics	Recommend	Recommend
Tecartus	\$533,523	Mantle cell lymphoma	Recommend	Recommend
Yescarta	\$485,021	Diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL)	Recommend	Recommend
Carvykti	\$632,455	Multiple Myeloma	Recommend	Recommend
Luxturna	\$1,031,500 (assuming treatment in both eyes)	Vision loss, inherited retinal dystrophy	Recommend	Recommend
Tecartus	\$533,500	Acute lymphoblastic leukemia	Recommend	Recommend
Kymriah	\$450,000	Relapsed or refractory follicular lymphoma	Recommend	Recommend
Yescarta	\$485,000	Relapsed or refractory follicular lymphoma	Recommend	Recommend

Note:

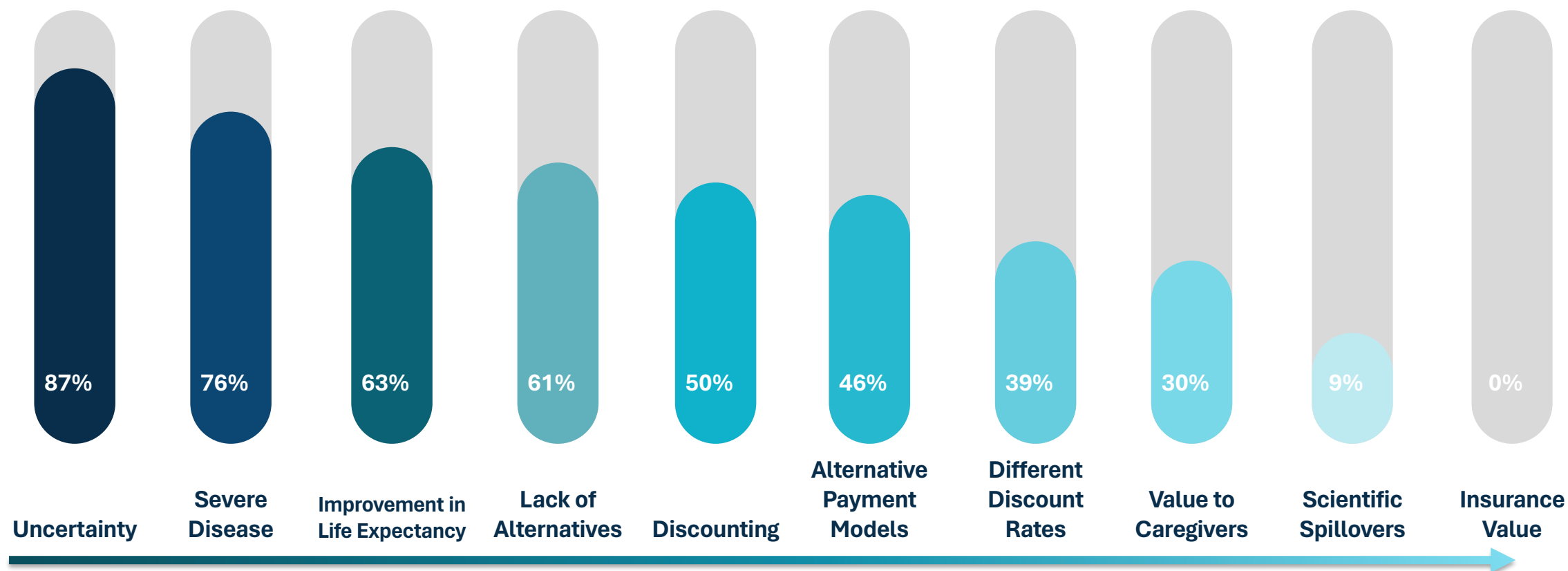
*Abecma was not recommended for reimbursement due to safety concern

**No file was closed without LOI at pCPA



There is a lot of variability in HTA considerations of economic evidence in assessing cell and gene therapies

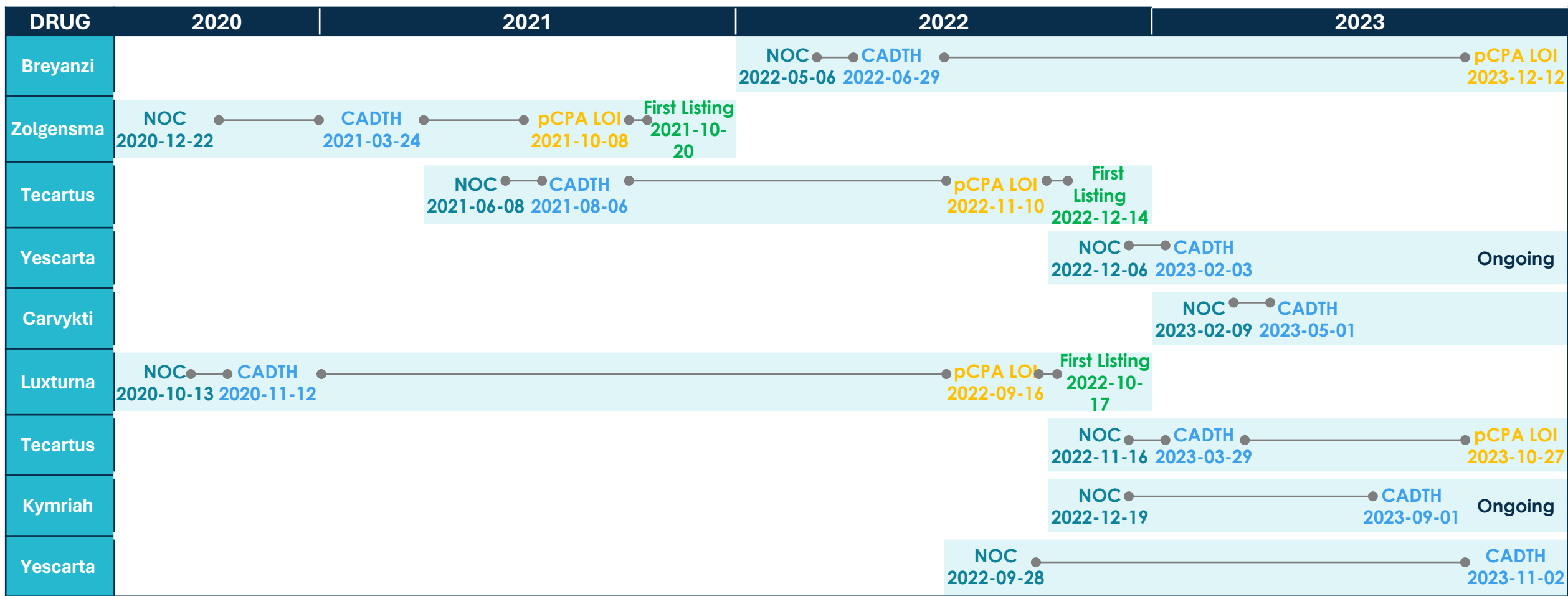
Consideration of various elements of economic evidence for Zolgensma across 7 HTA jurisdictions



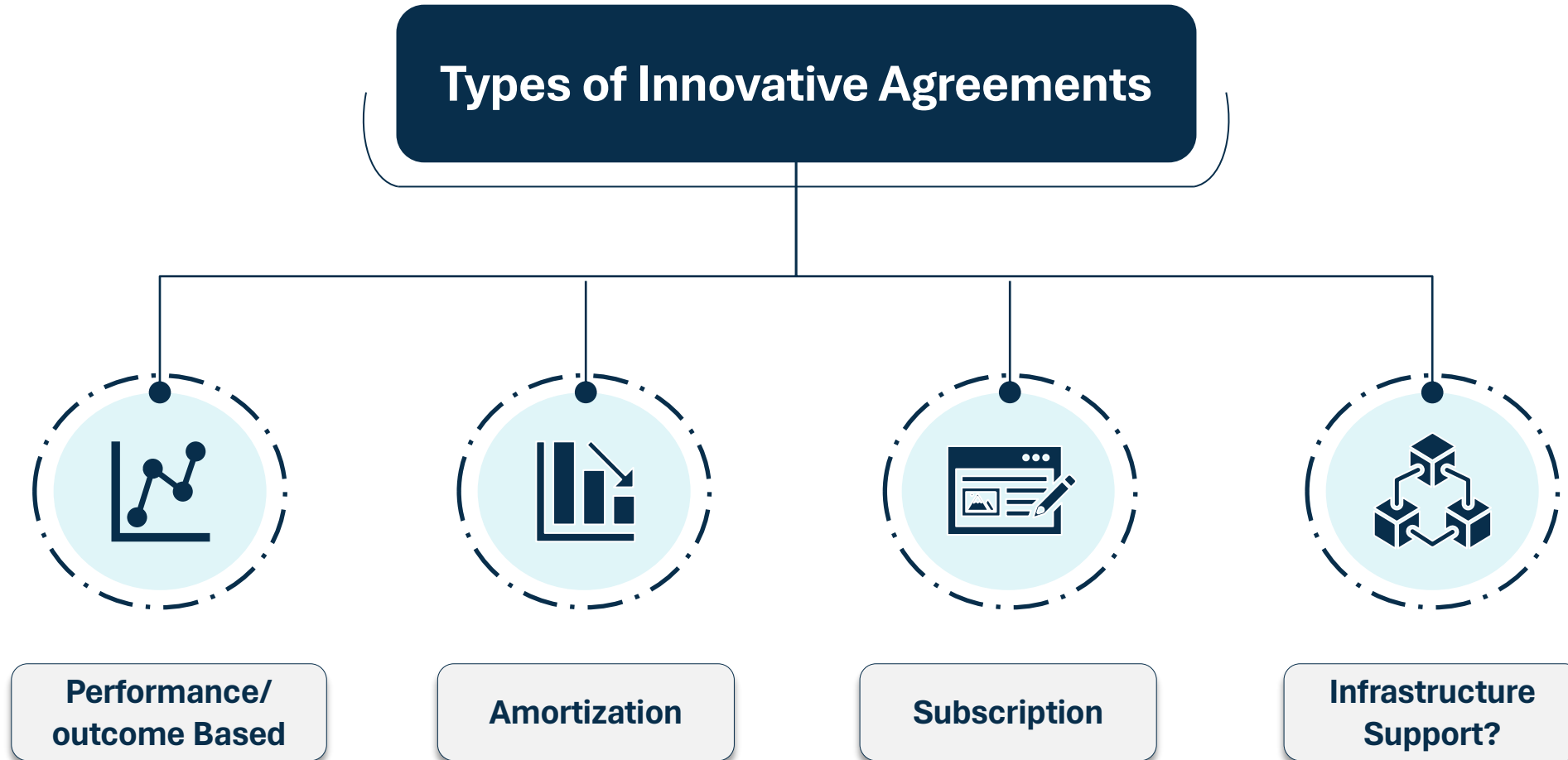


Reimbursement

Negotiation and implementation timelines have been challenging



Financing Challenges – Are Innovative Agreements Viable?





Implementation

Implementation differences within cell and gene therapies (ON)

	CAR-T	Luxturna	Zolgensma
Treatment Setting	 In-patient	 Hybrid	 Out-patient
Implementation / Budget	Special CAR-T Therapy Program	Ontario Health	Ontario Drug Programs: Exceptional Access Program
Therapeutic Area	 Oncology	 Non-oncology	 Non-oncology

- 2022 ON Budget: Ontario is investing \$162 million over three years to support additional cancer procedures and drugs, including \$26 million in 2022–23 CAR-T therapy to treat patients with different types of leukemia and lymphoma.
- OH Annual Report: The ministry approved Ontario Health’s provincial plan to fund Luxturna, a non-cancer gene therapy for adult and pediatric patients. By leveraging the existing infrastructure for provincial oversight of high-cost cancer drugs/therapies, Ontario Health is positioned to support the administration of non-cancer therapy funding.



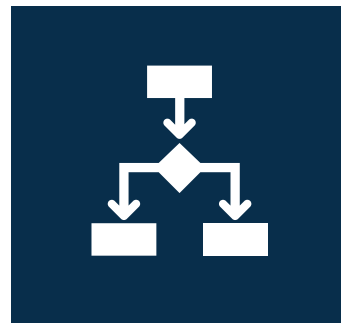
Building the future for supporting access to cell and gene therapies



Early Dialogue & Preparation



Equity



Implementation



Financing



Expertise & Infrastructure



Agile Procedures



Stakeholder Collaboration



Unique Pathways



Innovative Agreement



Education & System Investment





Thank you!



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6. Lee, SungKyung, and Jong Hyuk Lee. "Cell and gene therapy regulatory, pricing, and reimbursement framework: With a focus on South Korea and the EU." Frontiers in Public Health 11 (2023): 1109873.

