Cell & Gene Therapy Scientific Overview

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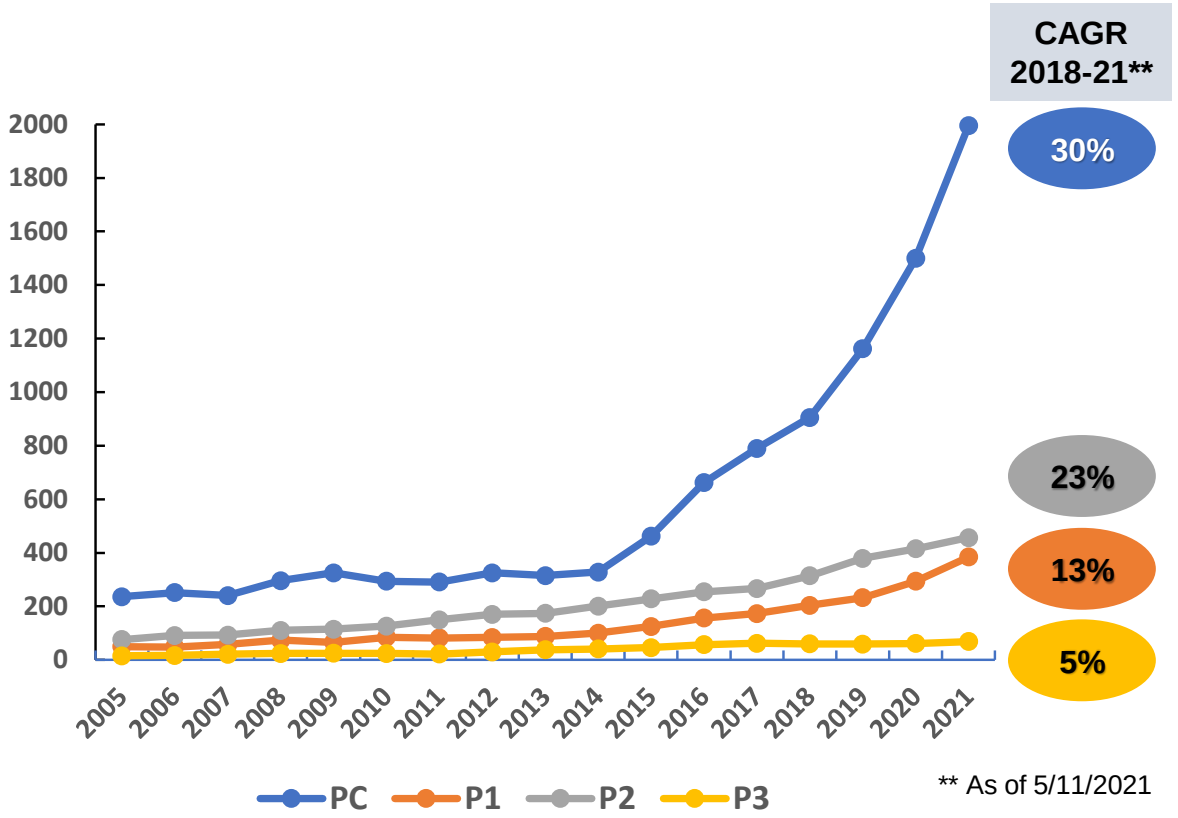
C&GT: Significant Growth Opportunity

C&GT Pipeline by Phase: >2,900 Active Programs



** As of 5/11/2021

Biopharma industry investing heavily in this class of research due to its **broad clinical application** to treat a wide range of **diseases with unmet needs**

9* **total** — Therapies approved by FDA today; Address key delivery, safety, and efficacy challenges

10-20 **per year** — **C&GT** expected to be approved per year by 2025

>900 — **Active programs** for C&GT in clinical trials worldwide

~80% — Programs in **Phase I or earlier**, setting the stage for massive growth

~200 — **IND** filings for C&GT expected to be received per year

~$20B — Funding for **C&GT companies** in FY 2020

Source: FDA, Association for Regenerative Medicine, PricewaterhouseCoopers, PharmaProjects, Citeline, SVB.
FDA: https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics
* Excludes cell transplantation and cell-based regenerative medicine products.

The Transformative Potential of Advanced Therapies

- **Advanced Therapeutic Medicinal Products (ATMPs)** are transformative medicines for human use
  - Based on genes, tissues, or cells providing new innovative treatments of disease and injury
  - Have the potential to be curative; currently control disease progression
  - Rapid development and commercialization, underpinned by biological understanding and early POC (proof of concept)

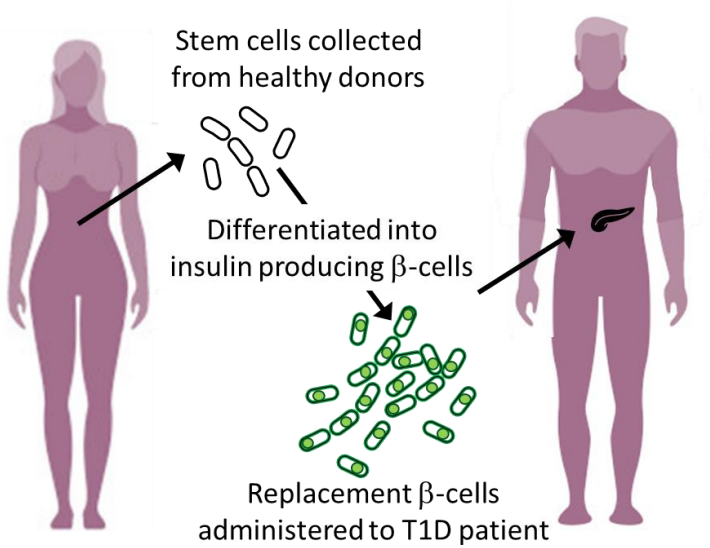
Gene Therapy	Cell Therapy	Gene-Modified Cell Therapy
Involves the introduction, removal or change in a person's genetic material to treat (or cure) a disease The new genetic content is usually transferred via a carrier or vector to the appropriate cells of the body	Involves the transfer of intact, live cells into a patient to treat (or cure) a disease The cells may be the patient's own (autologous) or those of a donor (allogeneic) The type of cell administered depends on the condition and relevant cell function	Involves BOTH protocols; cells are genetically modified with new genetic content outside of the patient, expanded to sufficient numbers, and then administered to the patient

Tackling a Range of Disease Types

Cell and gene therapies act to correct or address multiple disease-causing mechanisms

Cell Therapy

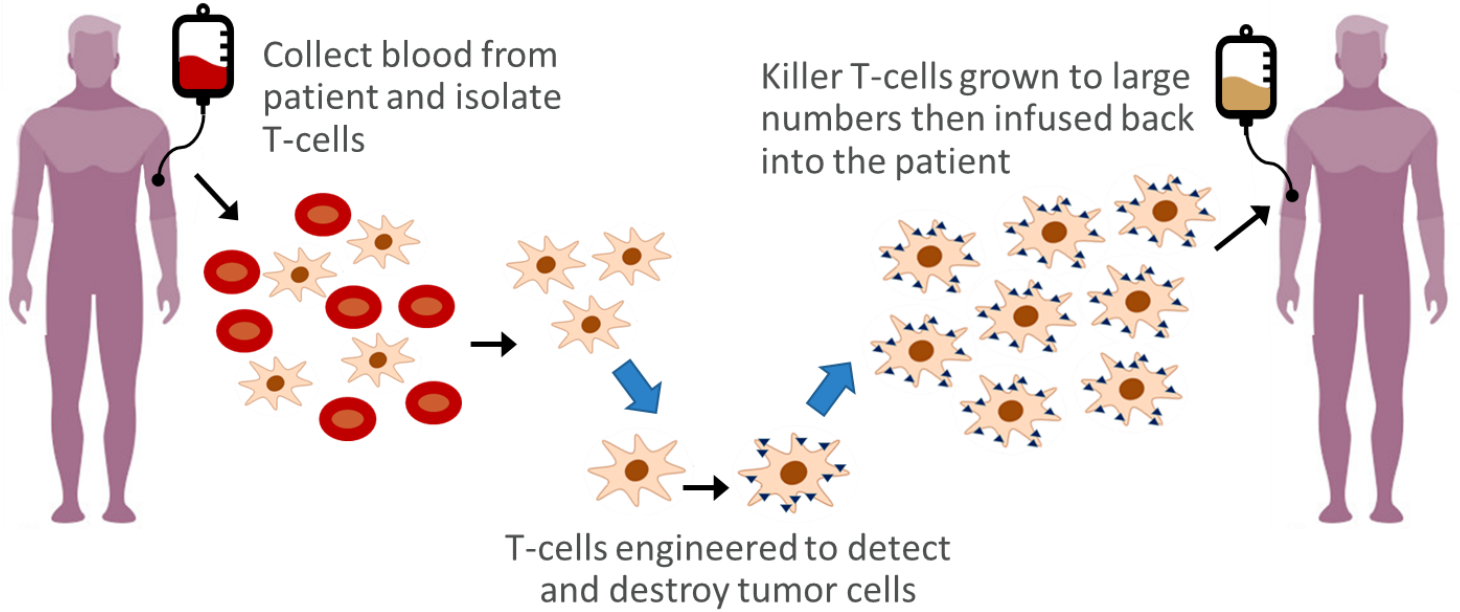
Cell donor cells implanted into tissues to reverse disease phenotypes



Type 1 Diabetes

Gene-Modified Cell Therapy

Immune cells directed to specific cell types (cancer) to kill and/or remove problem cells



Acute Lymphoblastic Leukemia (ALL)

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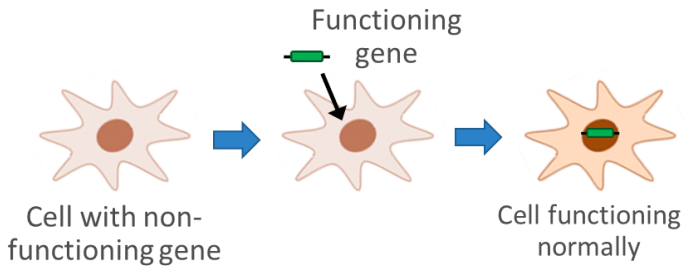
Tackling a Range of Disease Types

Cell and gene therapies act to correct or address multiple disease-causing mechanisms

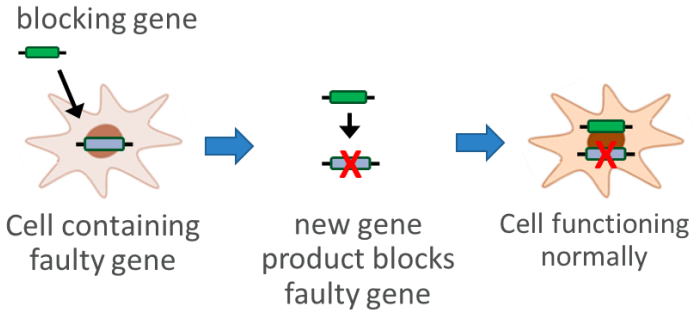
Gene Augmentation Therapy



Provides a functional copy of the faulty gene

- Inherited retinal diseases
- Cystic Fibrosis
- Spinal muscular atrophy

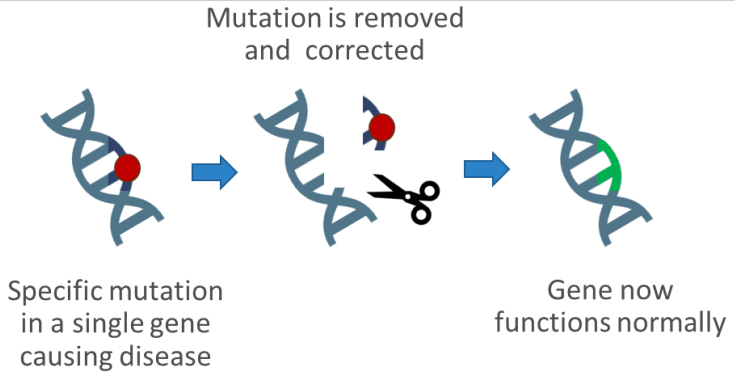
Gene Suppression Therapy



Turning off a gene that is not functioning properly

- Hereditary transthyretin-mediated amyloidosis (ATTR)

Gene Correction (Editing)



Targeted modification of a patient's genome to prevent or treat a disease

- Huntington's disease

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What Are Cell & Gene Therapies?

Advanced Therapeutic Medicinal Products (ATMPs)

Gene Therapy Medicines

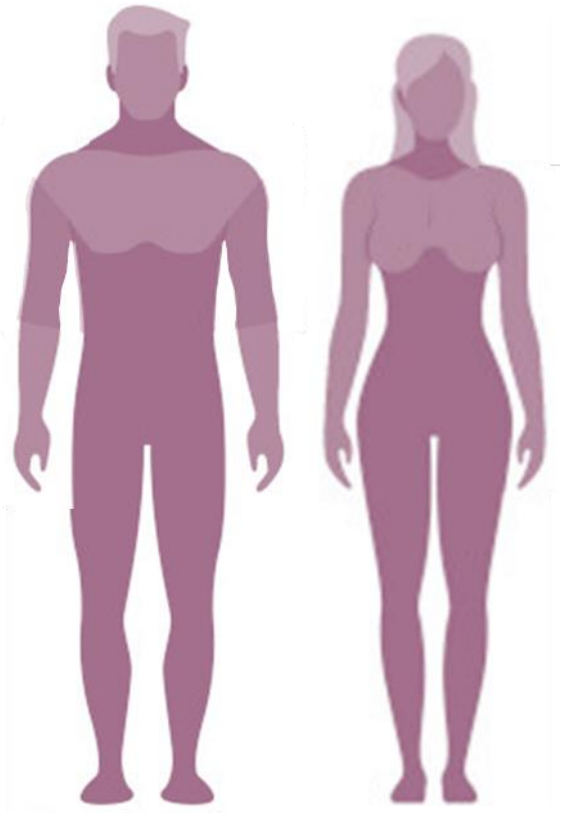
Non-viral vectors

Free in solution
(e.g. ‘naked’ DNA, mRNA)

Combined with delivery system (e.g. lipid / polymer-based)

Viral vectors

Gene delivered via a viral system (e.g. AAV/LV)



Cell Therapy Medicines

Genetically Modified Cell Therapy

Cells transduced with viral vectors to produce gene-modified cells
(e.g. CAR-T therapy)

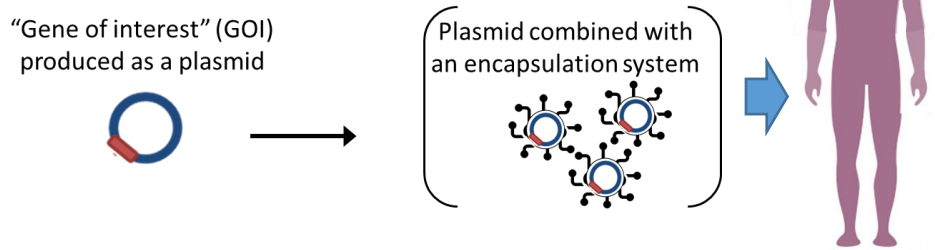
Non-Genetically Modified Cells

Cells extracted from a specific patient (autologous) or donor (allogenic)
(e.g. beta Cells T1D)

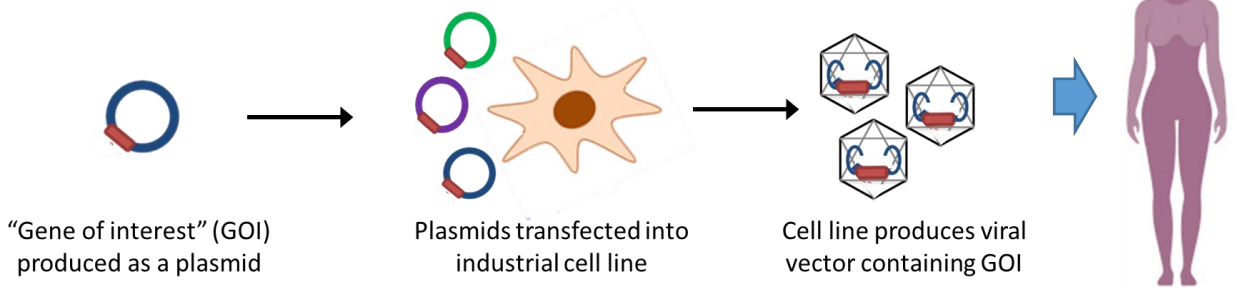
Direct Gene Therapies

A therapy that directly modifies a patient's genome

Non-viral Gene Therapy

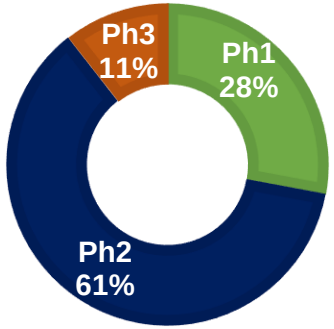


Viral Vector Gene Therapy



FDA-Approved Products

- 3 viral vector products
- No plasmid products (2 non-FDA approved)



Strong Clinical Pipeline

- >260 candidates globally

Clinical Pipeline Mix (2021)

- 58% are viral vector based
- 42% are non-viral vector based

DP — Materials/Tools — Design and Efficacy — Safety Assessment — Analytical Testing — Manufacture — DP

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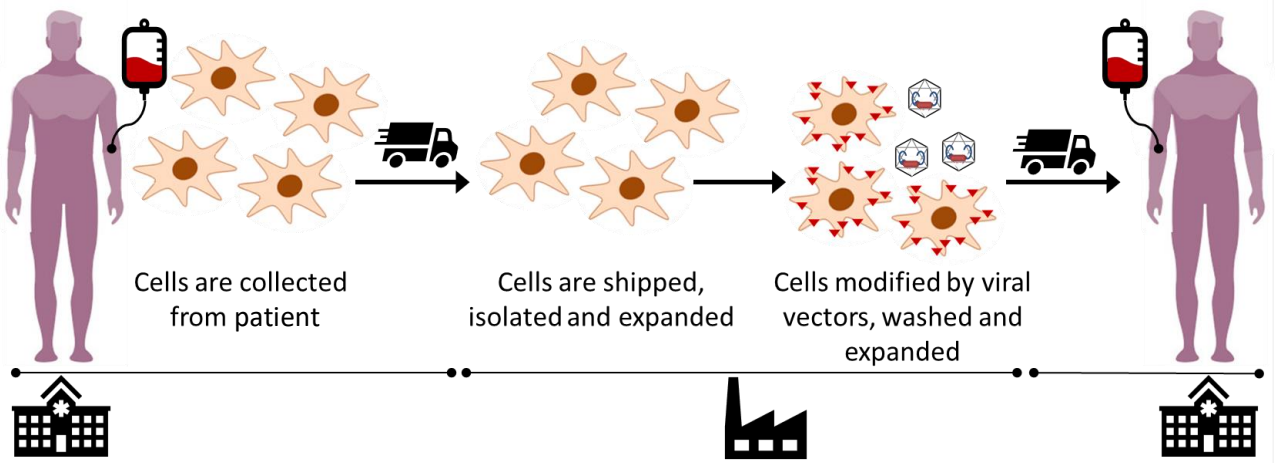
Autologous Cell-Based Therapies

Therapies that use a patient's own cells, modified to exert a therapeutic affect

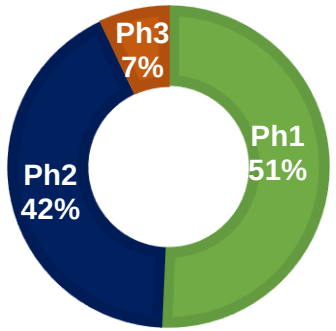
Ex vivo Gene-Modified Cell Therapy



Complex healthcare, logistical, and manufacturing supply chains requiring control and coordination

FDA-Approved Autologous Cell Products

- 5 gene-modified cell therapies; 1 cell therapies



Strong Clinical Pipeline

- >350 candidates globally

Clinical Pipeline Mix (2021)

- 70% of autologous cell therapy candidates are gene modified
- 30% are pure autologous cell therapy candidates

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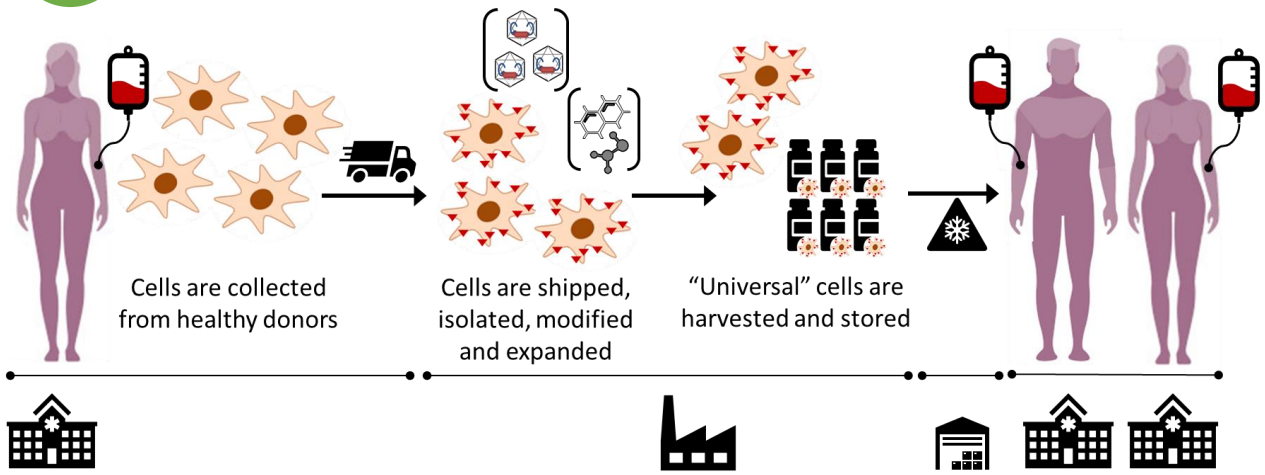
Allogeneic Cell-Based Therapies

Therapies that use cells from donors, that when modified exert a therapeutic affect to many

Allogeneic Cell Therapy

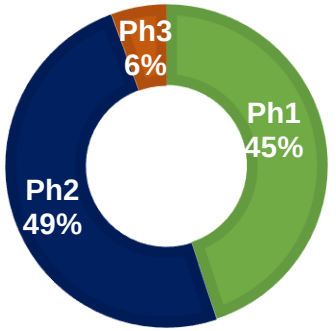


Enables the manufacture of "off-the-shelf" products, reducing the manufacturing cost burden

Sourcing material from screened healthy donors improves a product's safety profile and consistency

FDA-Approved Allogeneic Cell Products

- None yet
- 18 allogenic therapies in Phase 3 trials



Strong Clinical Pipeline

- >280 candidates globally

Clinical Pipeline Mix (2021)

- 40% of allogeneic cell therapy candidates are gene-modified
- 60% are pure allogeneic cell therapy candidates

DP — Materials/Tools — Design and Efficacy — Safety Assessment — Analytical Testing — Manufacture — DP

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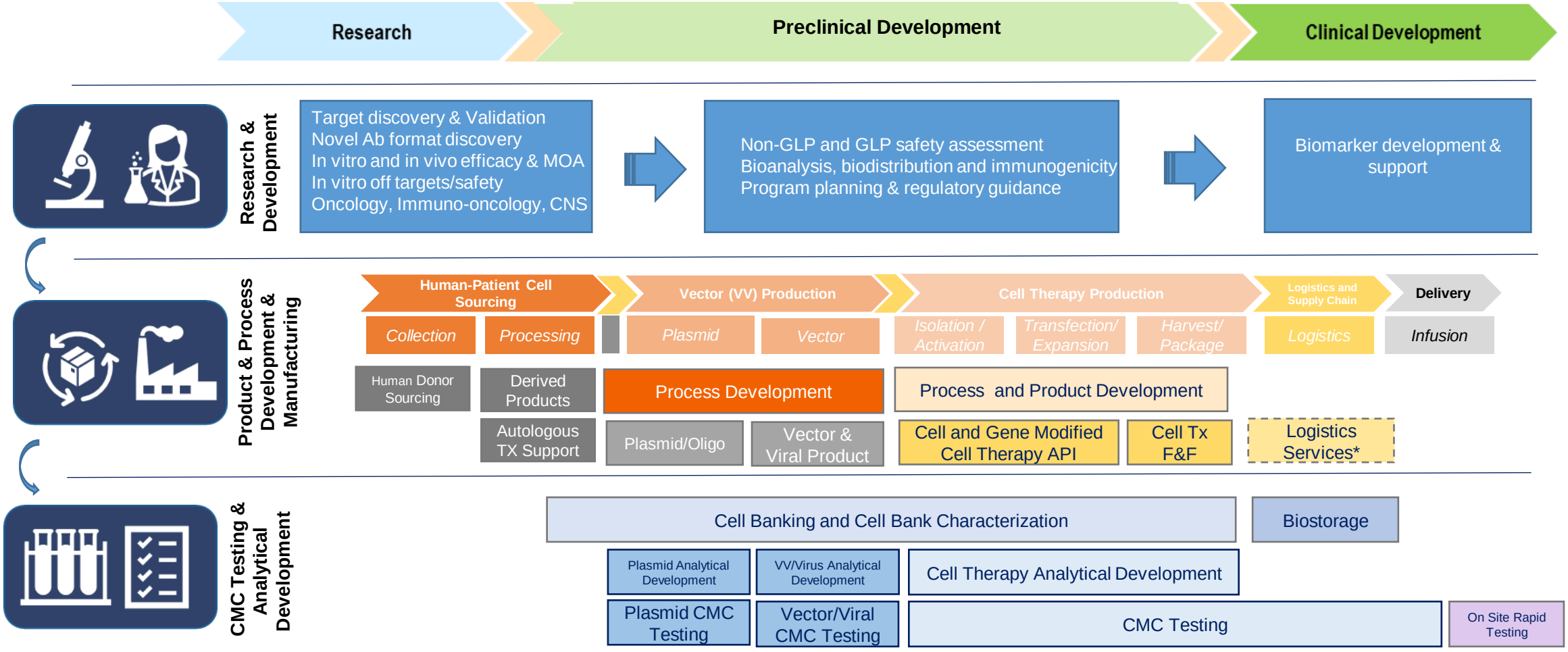
CRL: A Continuum of Products & Services for Advanced Therapeutics



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