Brooklyn ImmunoTherapeutics

A platform company in cell, gene-editing & cytokine therapies

mRNA Engineered Cell & Cytokine Medicines

September 20, 2021

Disclaimer

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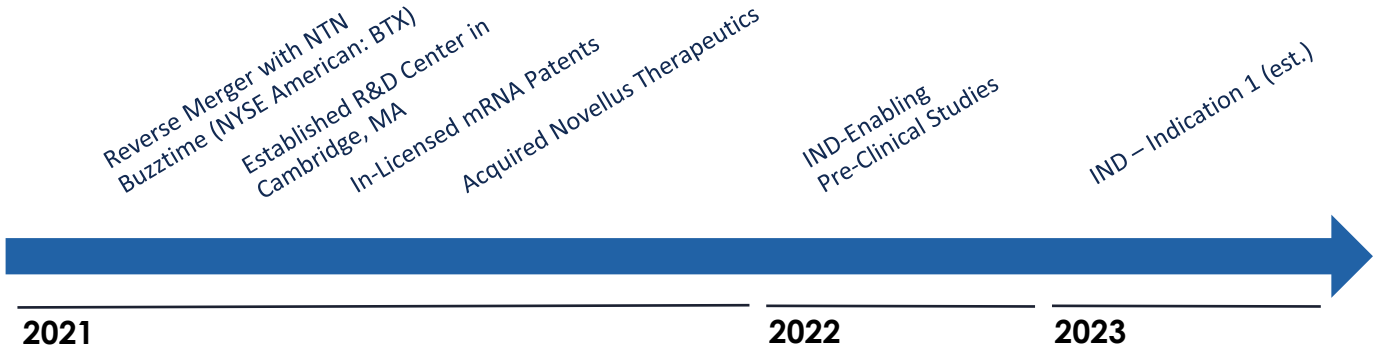
BTX: World's Only mRNA Cell-Engineering Platform

- What is mRNA cell-engineering? Messenger RNA (mRNA) is a special class of molecules that contain the instructions that determine how cells function. BTX's platform uses synthetic mRNA with minimized immune response to engineer cells to treat disease by repairing disease-causing mutations and directing the formation of stem cells.
- BTX is developing a platform of gene-editing and cell therapies based on exclusively in-licensed mRNA technology
  - Synthetic mRNA allows gene editing without provoking an immune response
  - mRNA therapeutics are safe and highly effective in patients
  - Fast to market – mRNA products have proven accelerated entry into clinical development
  - Low cost of goods sold – mRNA products avoid complex and costly viral-vector manufacturing
  - Can target any gene
  - No limit to the number or complexity of cellular modifications that can be made
  - Enables high-potency mRNA and precision cell therapies
  - Engineered cells are fully rejuvenated with greater expansion allowing more consistent treatments
- BTX's in-licensed vehicle safely delivers mRNA to cells inside and outside the body

BTX: Leveraging In-licensed Patent Portfolio to Advance Medicine

- BTX has an exclusive license from Factor Bioscience to a portfolio of granted patents around mRNA-based cell engineering that will provide BTX with a competitive advantage
- BTX's major platform components:
  - mRNA Cell Reprogramming (25 patents, extensive cellular data)
  - mRNA Gene Editing (15 patents, extensive cellular data)
  - NoveSlice™ Gene-Editing Protein (15 patents, extensive cellular data)
  - ToRNAdo™ mRNA Delivery Vehicle (4 patents, extensive cell and animal data)



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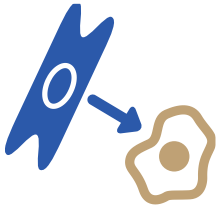
Brooklyn's Licensed mRNA-Based and LNP Technologies

Nucleic acid delivery

mRNA and LNP are the drug as in vivo gene-editing medicine



Cell reprogramming

Gene editing

mRNA and LNP are tools to make engineered cell medicine

Fields of Medicine Addressable with BTX Technology

mRNA-Gene Editing Medicine

Restoring function
single gene defects

Rebalancing
epigenetic loads

Correcting tumor
suppressor gene defects

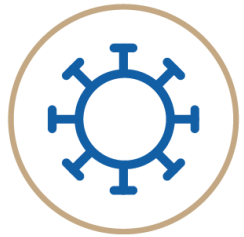
Repairing
somatic mutations

Blocking gain-of-function
toxic genes

mRNA Engineered Cell Medicine

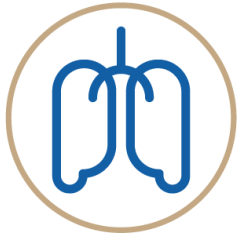
Cancer

Infectious diseases

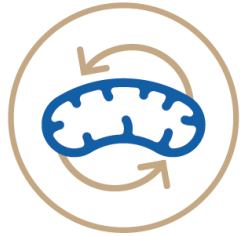


Autoimmune disorders

Respiratory disease



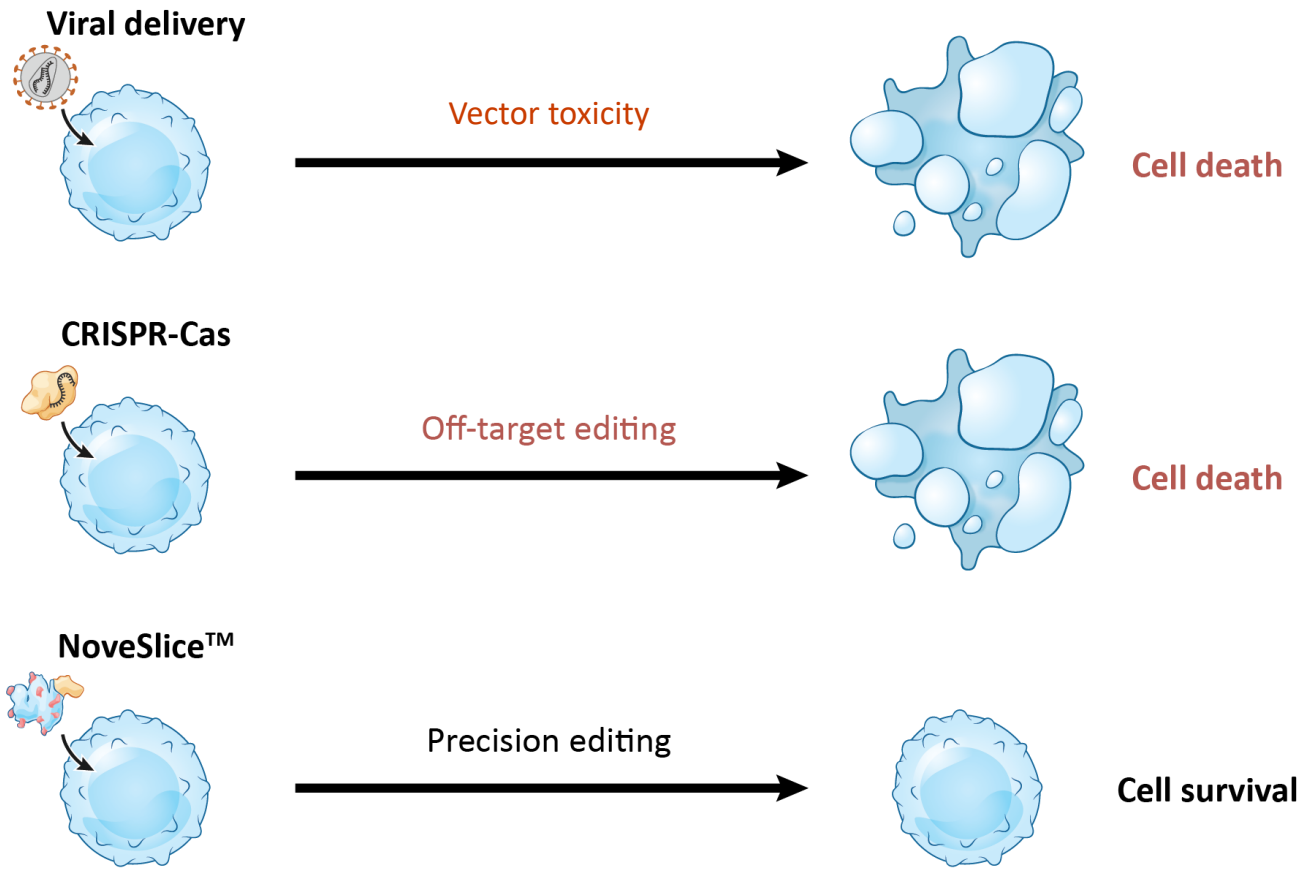
Metabolic diseases



Hormonal disorders

Neurological diseases

ToRNAdo™ Delivery Offers Superior Results



An Investment in BTX Today Offers Future Value

- Breadth and depth of BTX technology offer numerous opportunities for successful clinical results
- BTX in-licensed patent portfolio offers potential for licensing and royalty revenue in coming years
- BTX technology platform offers predictable path to clinical development, with initial clinical testing of cellular products expected within 2 years
- BTX patent portfolio offers range of clinical applications at low cost and low risk
- BTX legacy cytokine portfolio and completed Phase 2b trial offer additional value
  - Opportunity for partnering in the Ph3 registration study
  - Opportunity for advancing another Ph2 study in a different oncologic indication

BTX Technology: Competitive Landscape

	BTX	CRISPR[1]	TALENs[2]	Zinc-Finger Nucleases[3]	mRNA Vaccines[4]	CAR-T[5]
Primary Technologies	• mRNA Cell Reprogramming • mRNA Gene Editing • NoveSlice™ • ToRNAdo™	CRISPR (including base-editing)	TALENs	Zinc-Finger Nucleases	None	Viral Vectors for CAR-T
mRNA Gene Editing	Yes	Some	No	No	N/A	No
mRNA Cell Reprogramming	Yes	N/A	N/A	N/A	N/A	N/A
mRNA Delivery	Yes	Electroporation (limited to ex-vivo)	Electroporation (limited to ex-vivo)	Electroporation (limited to ex-vivo)	Vaccines	N/A
High Off-Target Effects	No	Yes (short gRNA recognition sequence)	Yes (based on plant-pathogen sequences)	Yes (requires extensive screening)	N/A	N/A
Immune response	No	Yes (bacterial protein)	Possible (plant-pathogen sequences)	Possible	Yes (desired for vaccines)	N/A
On-Target Efficiency	High	Medium	Medium	Medium	N/A	N/A
Cell Rejuvenation	Yes	N/A	N/A	N/A	N/A	N/A

Example Companies: [1] Beam Therapeutics, CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics. [2] Allogene Therapeutics, Cellectis, Iovance Biotherapeutics. [3] Sangamo Therapeutics. [4] BioNTech, Moderna. [5] Juno Therapeutics, Kite.

First Product Tier is a Stem Cell Product Platform

Mesenchymal Stem Cells (MSC)

- Multipotent stem cells capable of expansion and differentiation into different kinds of tissues
- Sources of trophic factors modulating the immune system and inducing repair of tissues

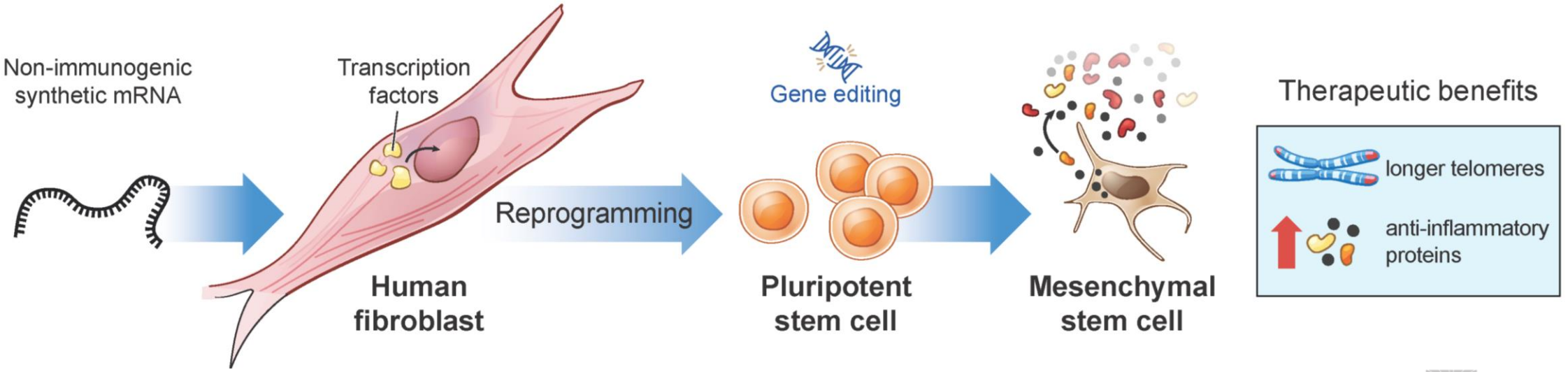
Product development leveraging extensive adult-derived MSC precedents

- Long history of clinical use and strong safety track record
  - Inconsistent or insufficient efficacy has plagued field, due product inconsistency or poor choice of clinical indication
- Well-described and long-practiced manufacturing
  - Multiple capable CDMO options exist
- A single Drug Product can be used across multiple and varied indications
  - Exploits homing/migration and anti-inflammatory properties of MSC

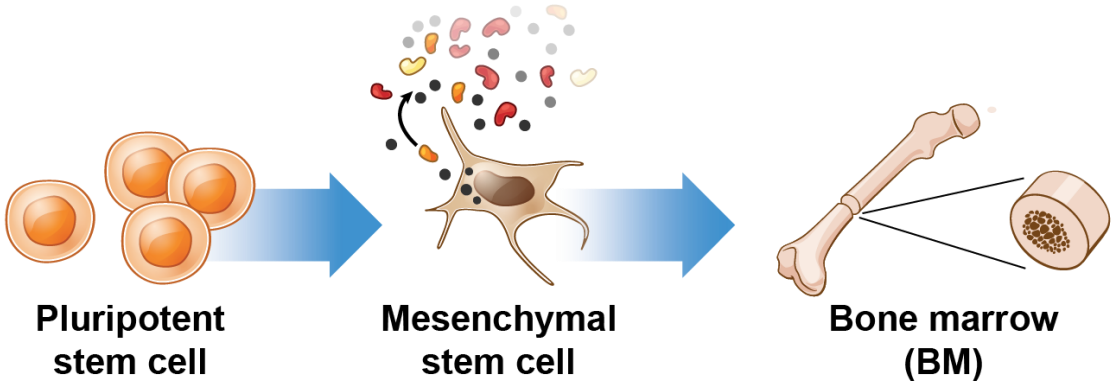
The iPSC Technology Addresses Issues with Adult Sources

iPSC-derived MSC advantages

- Amenable to more scaled manufacturing due longer proliferative life-span
  - One of the easiest iPSC-derived cell products to manufacture
- More consistent characteristics and improved therapeutic properties relative to adult sources
- Can gene edit the iPSC to program additional properties into iMSC and broaden therapeutic use

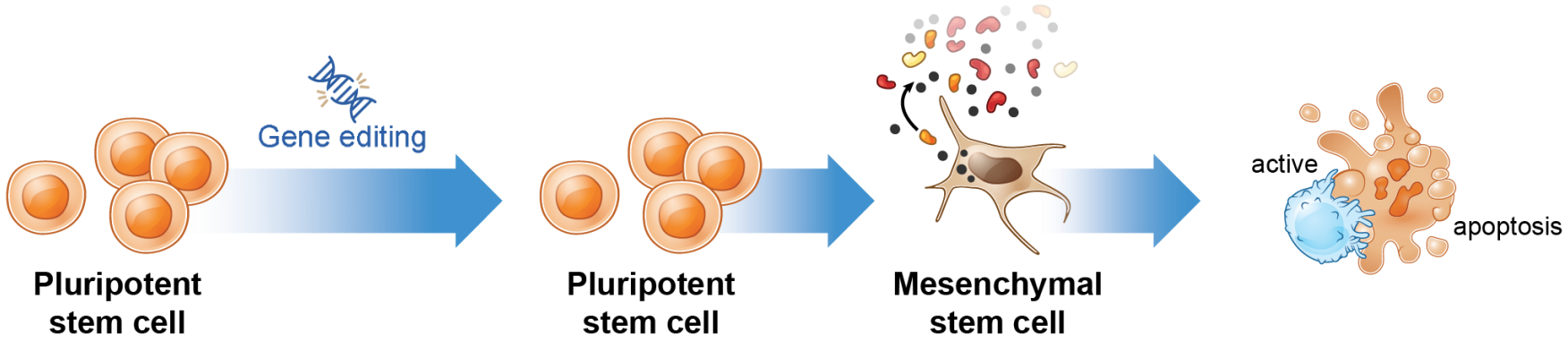


First Targeted Clinical Indication for iMSC Products



- Multiple clinical indications in setting of bone marrow transplant (BMT)
- Working with world class KOLs in BMT to focus on best clinical population(s) and trial design
- Preclinical development path elucidated by the iMSC program in ARDS (NoveCite partnership)

Developing Gene-edited Versions of iMSC Products Initially Targeting Poorly Addressed Solid Tumors



- Rationale for gene-edited iMSC in oncology
  - Harnessing MSC homing to tumors to locally deliver immune stimulating proteins
    - Addition of specific cytokines counters the pro-tumor effect that sometimes observed (i.e. anti-inflammatory properties of MSC)
- Rationale for IL-7 and IL-15 (members of IL-2 family)
  - IL-7/IL-15 used in vitro to enhance CAR-T tumor activity in vivo. Unlike IL-2, they will not induce proliferation of Tregs
  - Local delivery to tumor sites should reduce toxicities associated with systemic administration
- Targeting solid tumor clinical indications of high unmet need

Second Product Tier is a Genetic Medicine Product Platform

Proprietary lipid nanoparticle for nucleic acid delivery

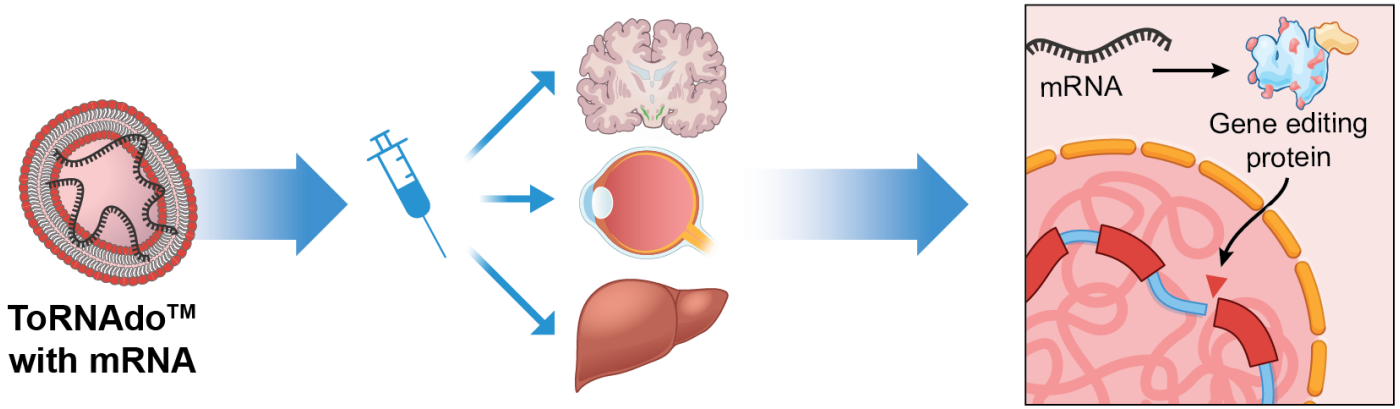
- Properties can be tuned to access different cell types and target tissues
- Can deliver RNA or DNA; facilitates gene correction approaches

Delivery of mRNA encoding for proprietary site-specific nuclease

- Nuclease can target any gene through design of protein binding domains
- High specificity to target genomic site
- Achieves high level but transient expression of nuclease, enhancing safety

Developing In Vivo Gene-editing Products Addressing Rare Disease Indications (Orphan Designation)

- Direct gene editing in the liver, brain or eye for monogenic disorders
- Ability to knock-out or correct the target gene
- Initial gene targets include
  - *TTR* for Familial Transthyretin Amyloidosis (ATTR)
  - *ABCA4* for Stargardt Disease (monogenic form of macular degeneration)



ToRNAdo™ is a trademark of Factor Bioscience Inc.

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Third Product Tier is a Personalized Cell Therapy Platform

Licensed technology is the safest, most efficient, and fastest method for iPSC derivation

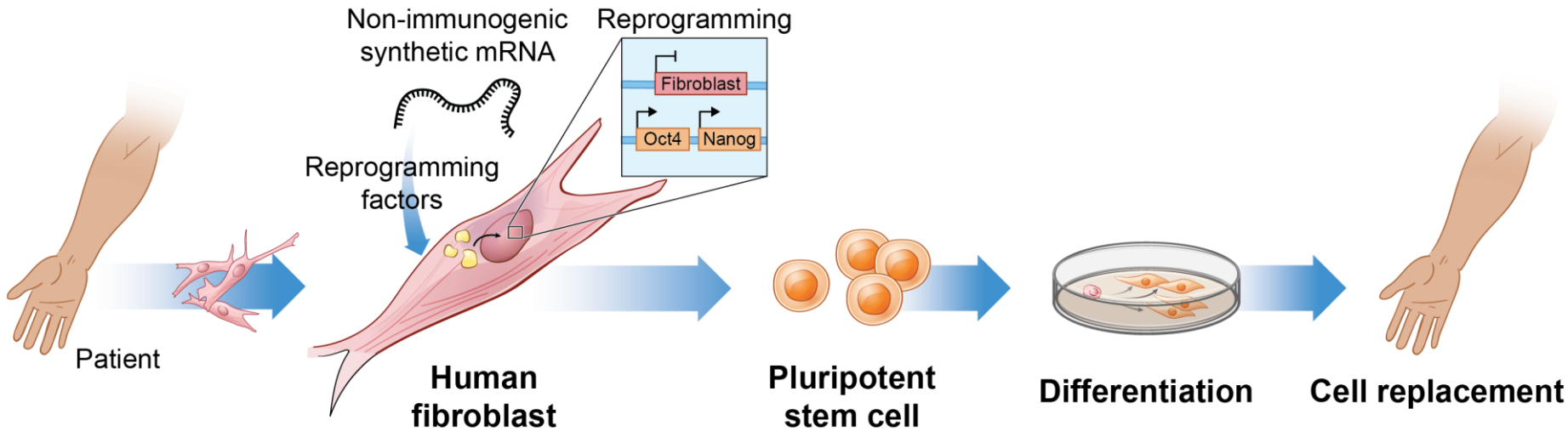
- Safe: Non-integrating method using synthetic mRNA to produce reprogramming factors
- Efficient: Uses LNP for repeated in vitro delivery with low toxicity
- Efficient: Can combine reprogramming and gene editing in single step derivation
- Fast: Reprogramming and iPSC colony formation within 2 weeks

The safety, reliability and speed enable autologous iPSC programs

- Efficiency of reprogramming permits low quantity of cells from biopsy and simultaneous correction of gene defects
- Can quickly produce multiple iPSC clones per patient
- Absence of genome integration facilitates screening to identify and characterize a safe clone

Autologous Cell Therapy Applications of Licensed Technology

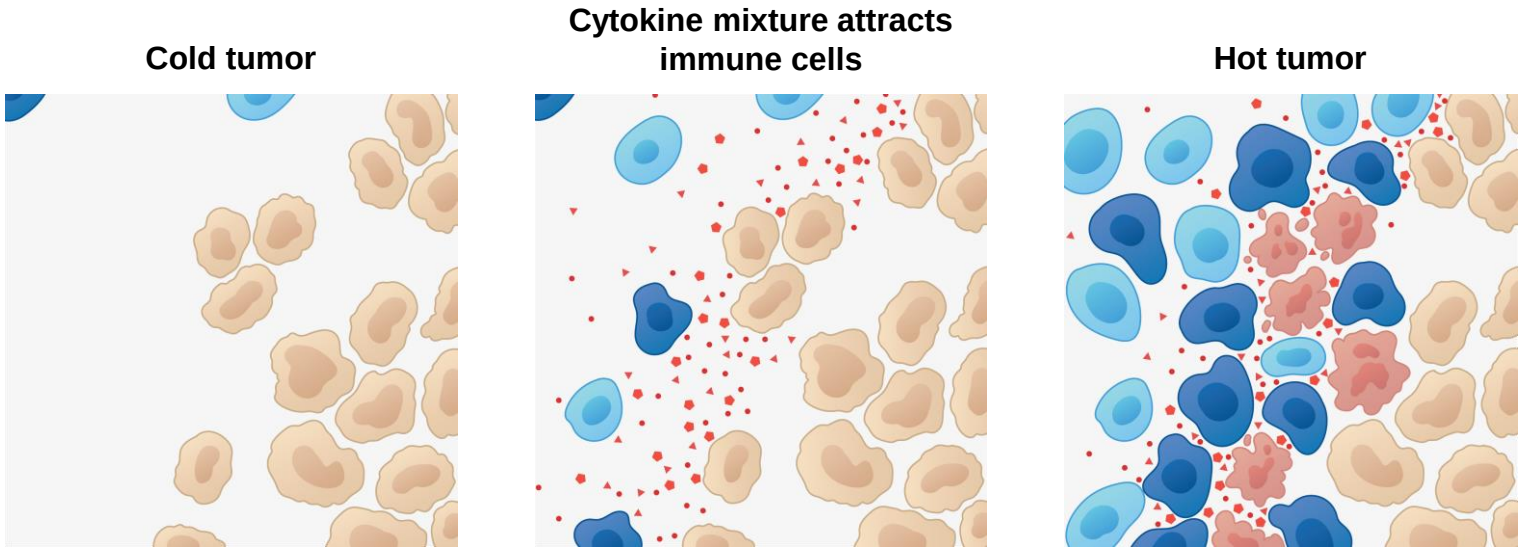
- Autologous iPSC / Gene-modified autologous iPSC for:
  - Genetic disease (e.g. Sickle cell disease)
  - Infectious disease (e.g. HIV)
  - Other cell therapy indications
- Autologous programs represent opportunities for future BTX expansion or partnering



BTX Cytokine, Cell Therapy, and Gene Editing Pipeline

Indication	Approach	Discovery	Preclinical	IND-enabling	Early clinical	Late clinical	Comments
IRX-2: human cell-derived mixed cytokine							
Head & Neck Cancer	SubQ injections						Phase 2b
Various IST	SubQ injections						Phase 1/2
iMSC: iPSC-derived mesenchymal stem cells							
ARDS	I.V. injection						NoveCite program
BMT failure	I.V. injection						
TBD (inflammation, autoimmunity)	I.V. injection						
TBD (inflammation, autoimmunity)	other than I.V.						
Solid tumors	Gene-edited (IL-7 + IL-15)						
In vivo gene editing							
Transthyretin Amyloidosis	I.V. or CNS						
Stargardt Disease	Retinal injection						

IRX-2 Mixed Cytokine Product Invigorates the Immune Response to Tumors



- Multiple cytokines in mixture can act locally and potentially in systemic fashion
- Human cell-derived source addresses toxicity observed with other IL-2 cancer therapies
- Currently in Phase 2b for Neoadjuvant Head and Neck Cancer, data readout in 1H-2022

BTX Most Advanced Asset: IRX-2 Human-Derived Cytokines

Currently in Phase 2b for Neoadjuvant Head and Neck Cancer *Final data readout expected in 1H2022*

Additional Investigator Sponsored Trials (ISTs) in:

- Renal Cell Cancer
- Liver Cancer
- Head and Neck Cancer
- Gastrointestinal Cancer
- Cervical/Vulvar Interstitial Neoplasia
- Triple Negative Breast Cancer
- Early Stage Breast Cancer

Future Planned Studies:

- Phase 2 Company Sponsored Study in 1 IST Indication targeted to begin in 2022
- Phase 3 Study in Neoadjuvant Head and Neck Cancer targeted to begin in 2023

Strong IP and Patent Position

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