



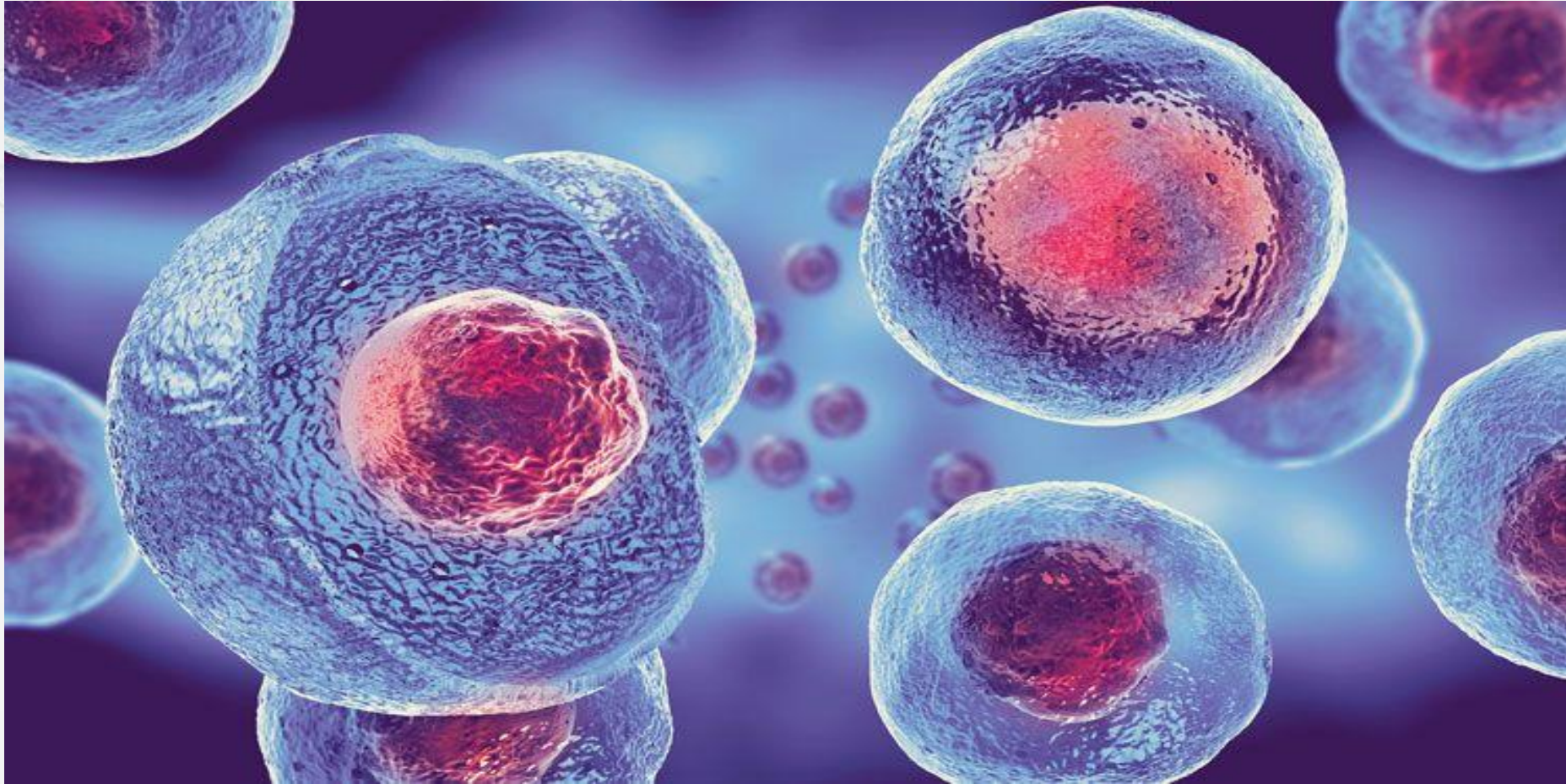
Cell Therapies that cure

May 2024 (TASE: KDST)

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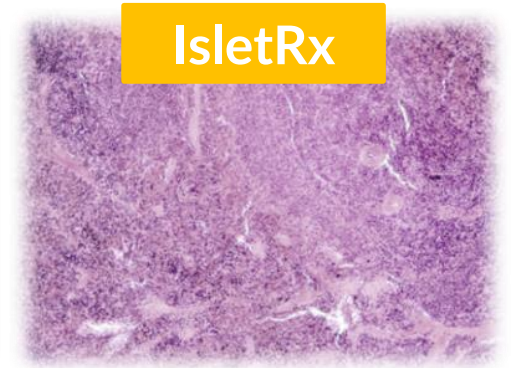
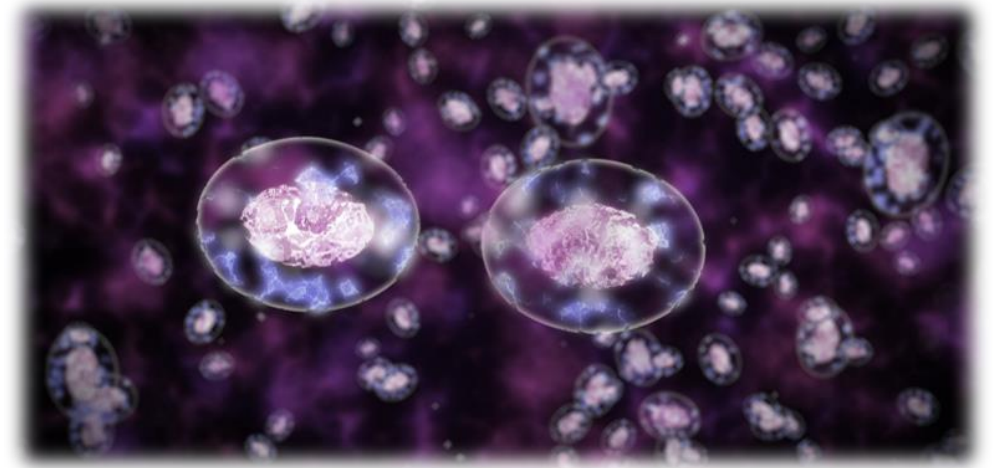
Kadimastem – Stem Cell Derived Cell Therapy



Vision – Stem Cell Derived Cell Therapy

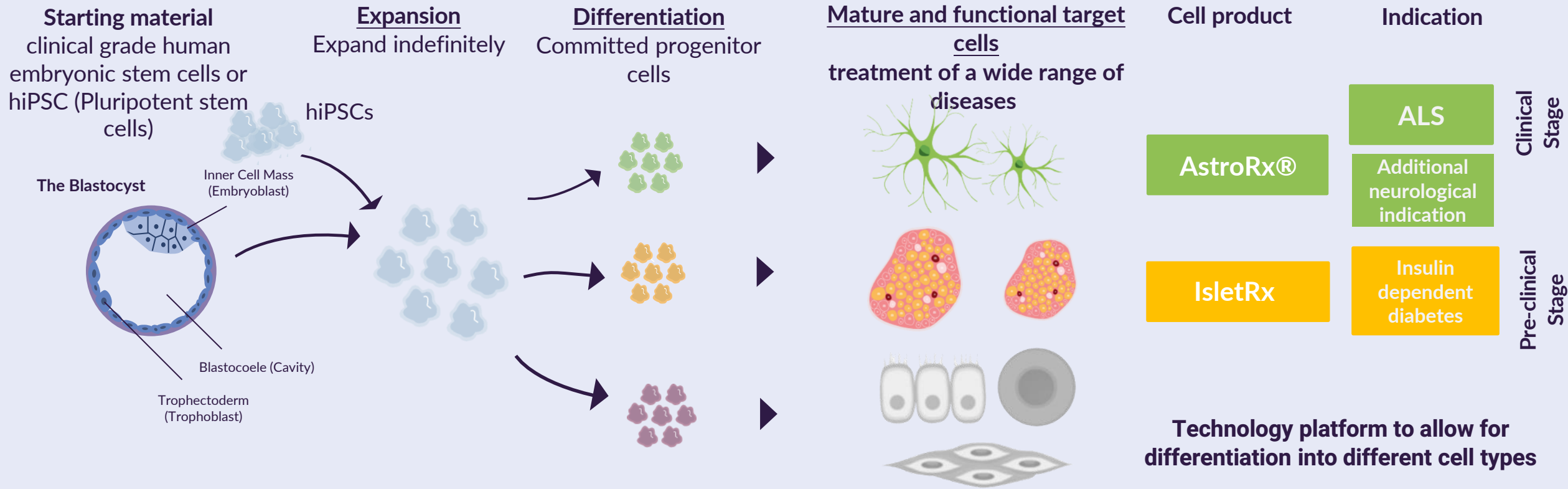
To Replace, restore and repair the functionality of diseased and malfunctioning cells in various degenerative diseases by transplantation of healthy and functional cells

Developing proprietary cell lines optimized for the cure of **Diabetes** and to treat **ALS**



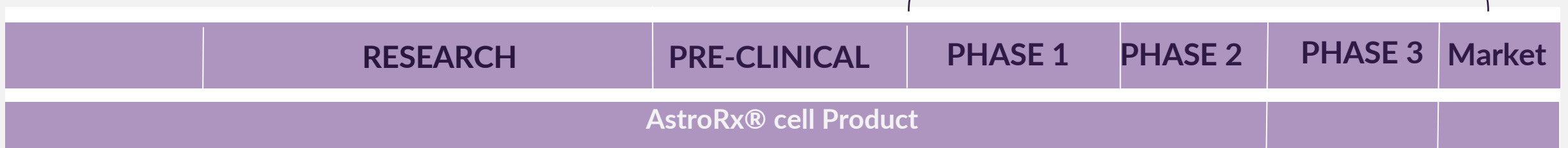
Proprietary Innovative Platform

Proprietary expansion and differentiation processes of cells intended for treatment of multiple diseases



Product Platform Pipeline

CLINICAL



Neurology

ALS - demonstrated encouraging results in the clinical trial

Multiple Sclerosis

Other NDD indications

Other NDD

NDD = Neurodegenerative Diseases

- ✓ Orphan drug designation (FDA)
- ✓ Completed Phase I/IIa (Israel)
- ✓ FDA approved IND for phase IIa clinical trial

Next:

- 2025 – Readiness to Phase IIa Clinical Trial in the USA



Diabetes (Insulin dependent)

1st Generation - Microencapsulation

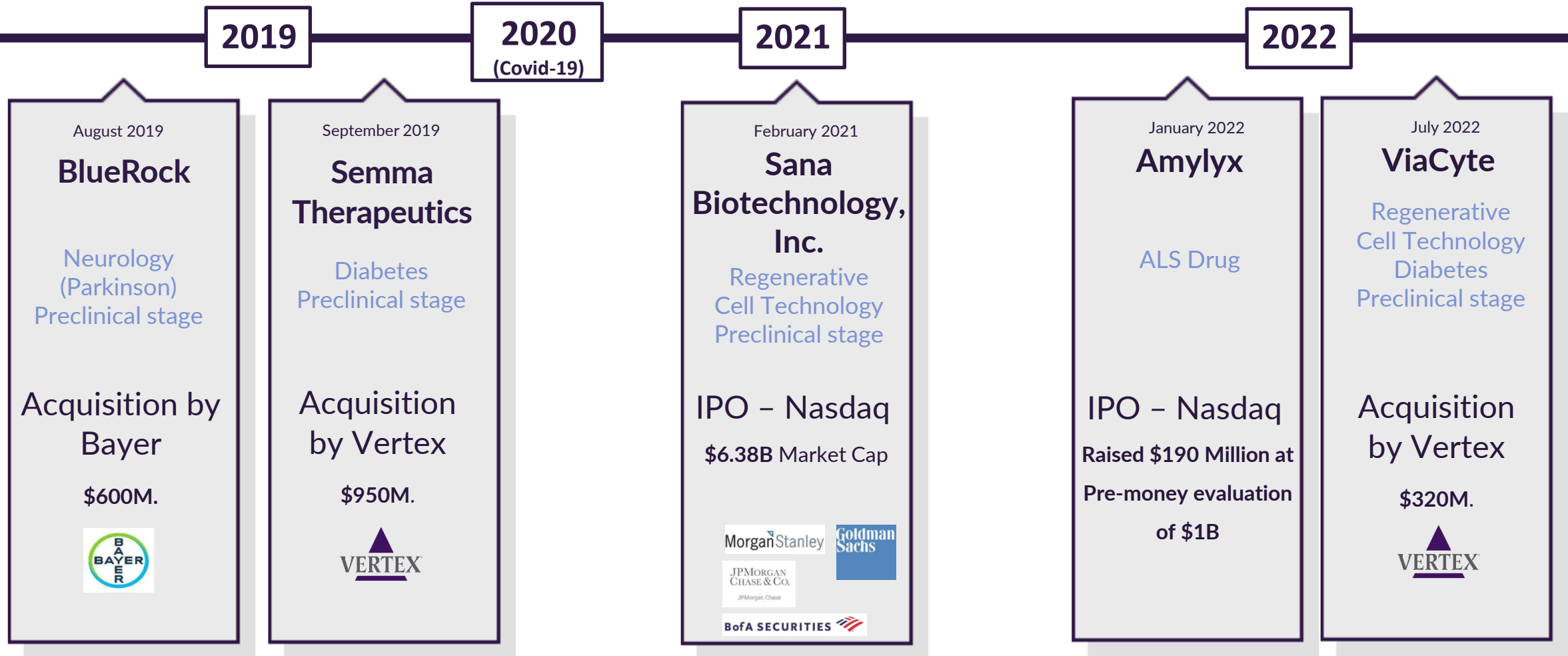
2nd Generation - collaboration

- ✓ Patented sorting and purification technology
- ✓ INTERACT with the FDA

Next:

- Q4 2024 - Pre-IND
- Immune protection through collaborations

An Active Market – Key Recent Transactions

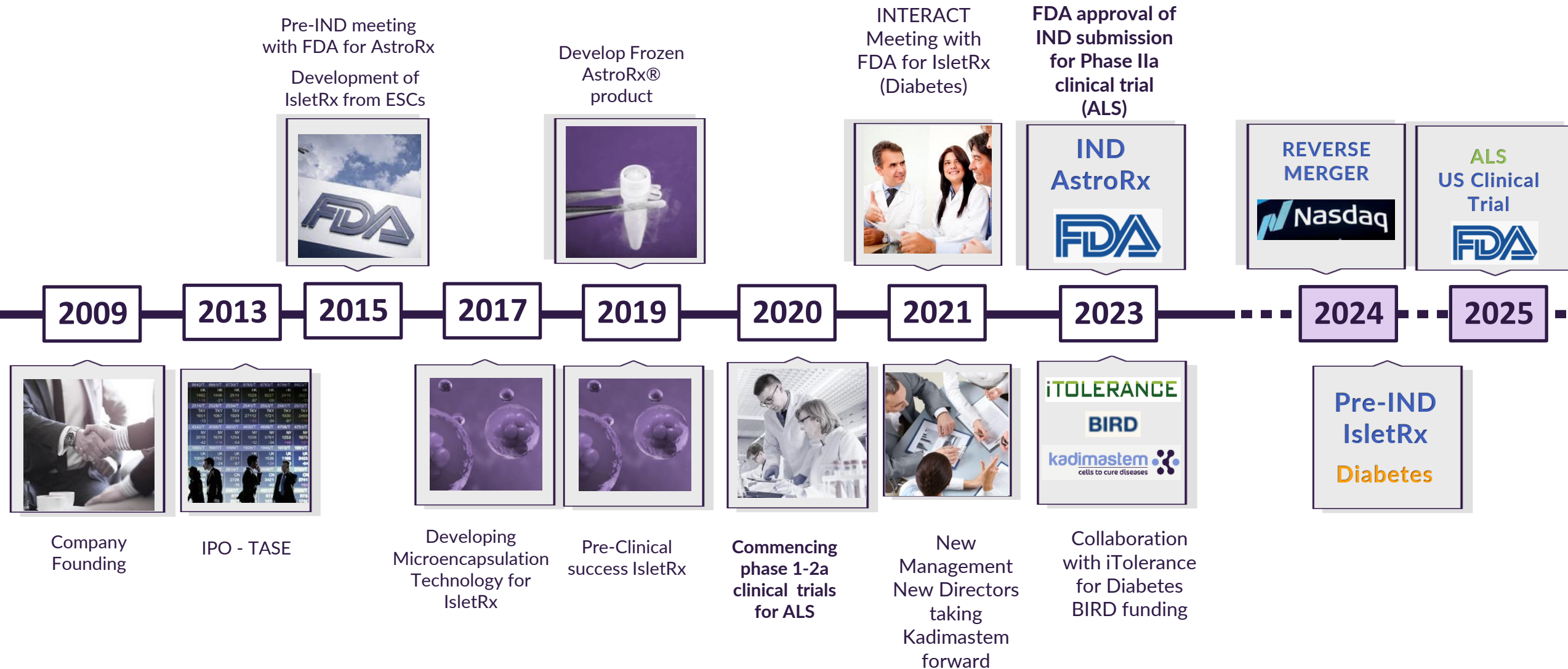


To the best of Company's knowledge, base on the following:

- <https://investors.vrtx.com/news-releases/news-release-details/vertex-acquire-semma-therapeutics-goal-developing-curative-cell>
- <https://www.prnewswire.com/news-releases/lilly-and-sigilon-therapeutics-announce-strategic-collaboration-to-develop-encapsulated-cell-therapies-for-the-treatment-of-type-1-diabetes-300624199.html>
- <https://www.bayer.com/media/en-us/bayer-acquires-bluerock-therapeutics-to-build-leading-position-in-cell-therapy/>
- [https://www.reuters.com/article/idUSKBN2A42JA/#:~:text=\(Reuters\)%20%2D%20Shares%20of%20gene,market%20capitalization%20of%20%246.38%20billion.](https://www.reuters.com/article/idUSKBN2A42JA/#:~:text=(Reuters)%20%2D%20Shares%20of%20gene,market%20capitalization%20of%20%246.38%20billion.)
- <https://stockanalysis.com/stocks/amlx/market-cap/https://companiesmarketcap.com/celularity/marketcap/>
- [Amylyx Pharmaceuticals Announces Pricing of Upsized Initial Public Offering of Common Stock\[1\].pdf](https://www.amylyx.com/news/amylyx-pharmaceuticals-announces-pricing-of-upsize-initial-public-offering-of-common-stock)



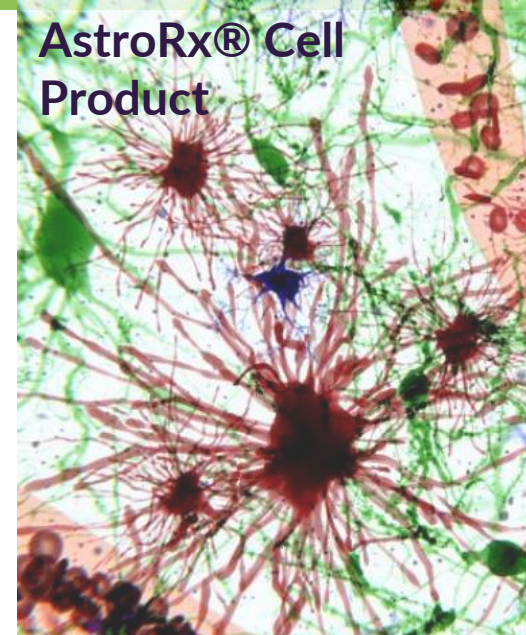
Kadimastem: History & Way Forward



AstroRx®

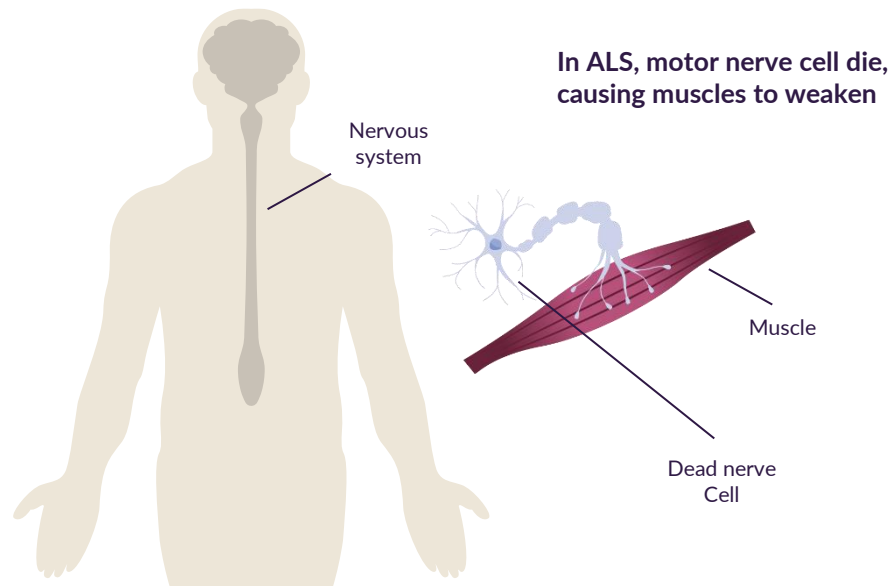
Astrocytes- Cell Therapy Treatment for Neurodegenerative Diseases

AstroRx® Cell
Product



ALS– Market and Facts

- Death of motor neurons
- Progressive loss of muscle control leads to eventual death
- 90-95% sporadic and 5-10% familial (C9orf72, hSOD1, TDP-43, FUS)
- Disease onset 45-65 years, survival from onset of 2-5 years



- Current FDA approved treatments are Rilutek, Radicava and RELYVRIO with modest effect

- Around **450,000¹** ALS patients estimated worldwide, **30,000** patients in the US²
- **Global ALS treatment market valued at US\$300 million in 2023³**

North America is the largest market, with a share about 60%, followed by Japan, and Europe, both have a share over 20 percent.

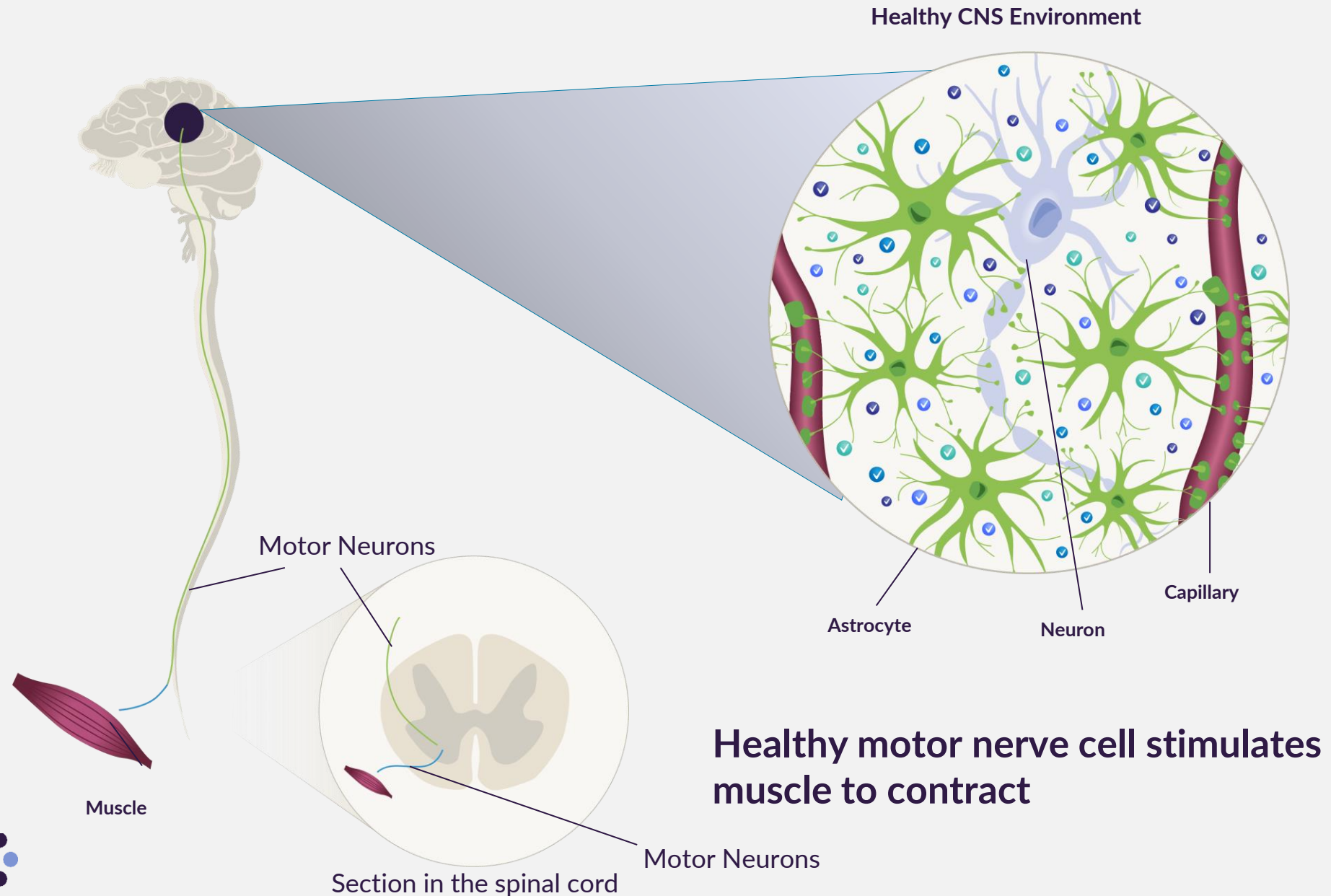
Estimate to reach in 2030: \$520.8 M³

- **US ALS Healthcare costs:**
Close to \$1.02 billion annually direct and indirect associated costs⁴.



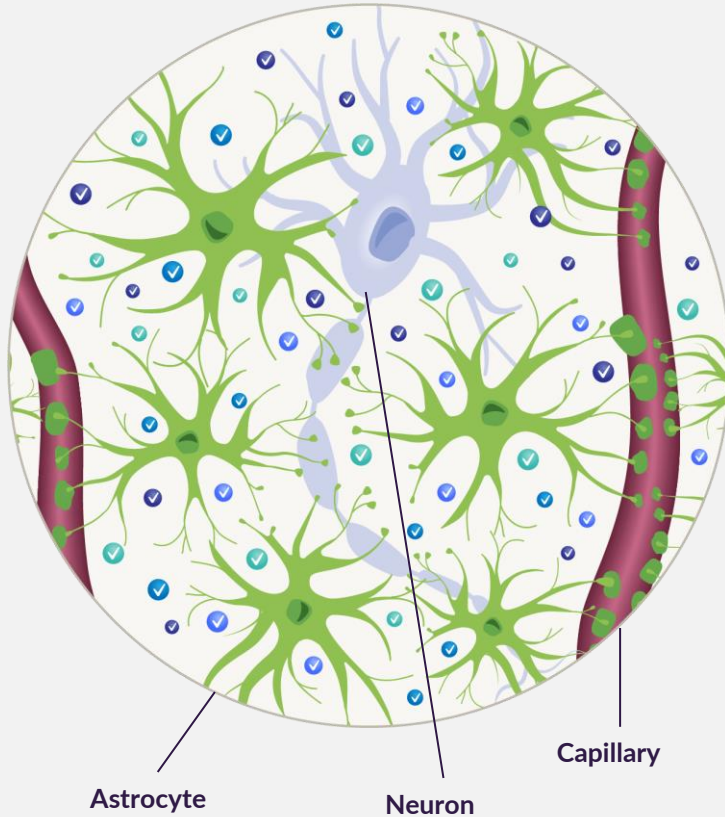
1. <https://www.massgeneral.org/neurology/als>
2. <https://www.als.net/als-resources/faq/>
3. <https://www.360marketupdates.com/global-amyotrophic-lateral-sclerosis-als-treatment-market-27075231>
4. <https://www.tandfonline.com/doi/full/10.1080/21678421.2023.2165947>

The Central Nervous System

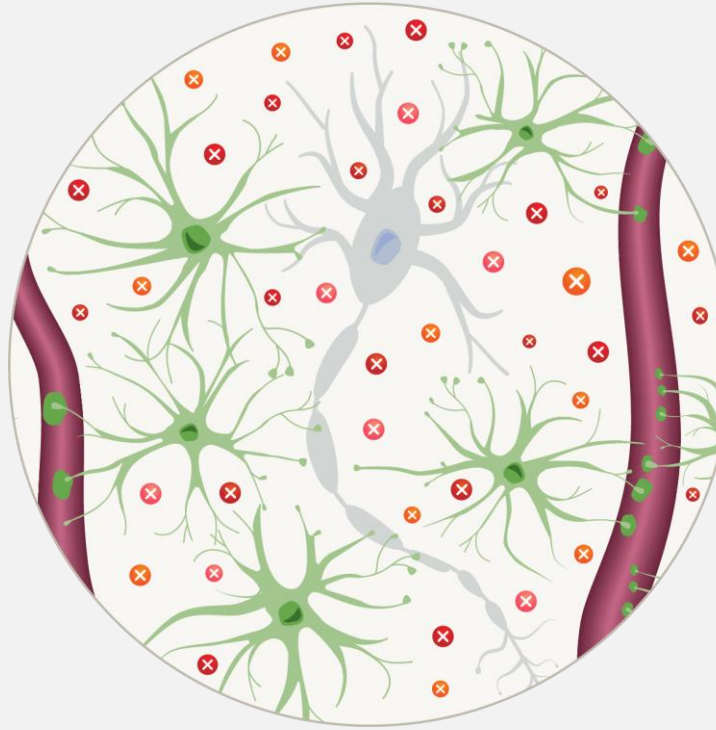


Use Astrocytes for ALS - AstroRx®

Healthy CNS Environment

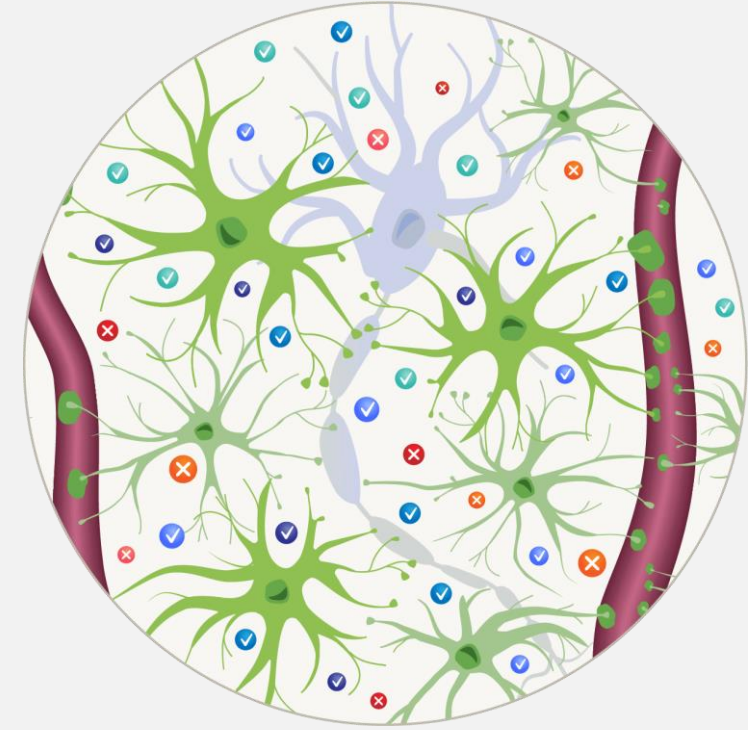


ALS Patients' CNS Environment



Astrocytes malfunction in ALS

Injecting AstroRx®
Healthy, Functional Astrocytes in
the CNS



AstroRx® Support motor neurons by
secreting neurotrophic factors and
clearing toxic environment

Why Use Astrocytes for ALS - AstroRx[®]

AstroRx[®] contains functional healthy astrocytes to protect ALS-diseased motor neurons using multiple mechanisms of action

In ALS, the patient's own astrocytes fail to support motor neuron survival	Mechanism of Action	ALS Patients' Astrocytes	AstroRx [®] Healthy, Functional Astrocytes
	Secrete neurotrophic factors ¹	✗	✓
	Remove toxic factors (i.e. glutamate) ¹	✗	✓
	Regulate oxidative stress ¹	✗	✓
	Immune-modulation ²	✗	✓

1. Izrael et al, 2020 Front Neurosci. 2020; 14: 824. doi: 10.3389/fnins.2020.00824

2. Izrael et al, 2021 Front Med (Lausanne) 2021; 8: 740071. doi: 10.3389/fmed.2021.740071

Effect of AstroRx® on rat SOD1^{G93A} ALS model

In Pre-Clinical Trials

Rat hSOD1 ALS Model:

Study measurements

- Survival
- Grip strength
- Rotarod (ambulation)
- Muscle weight loss
- Paralysis (neurological score)

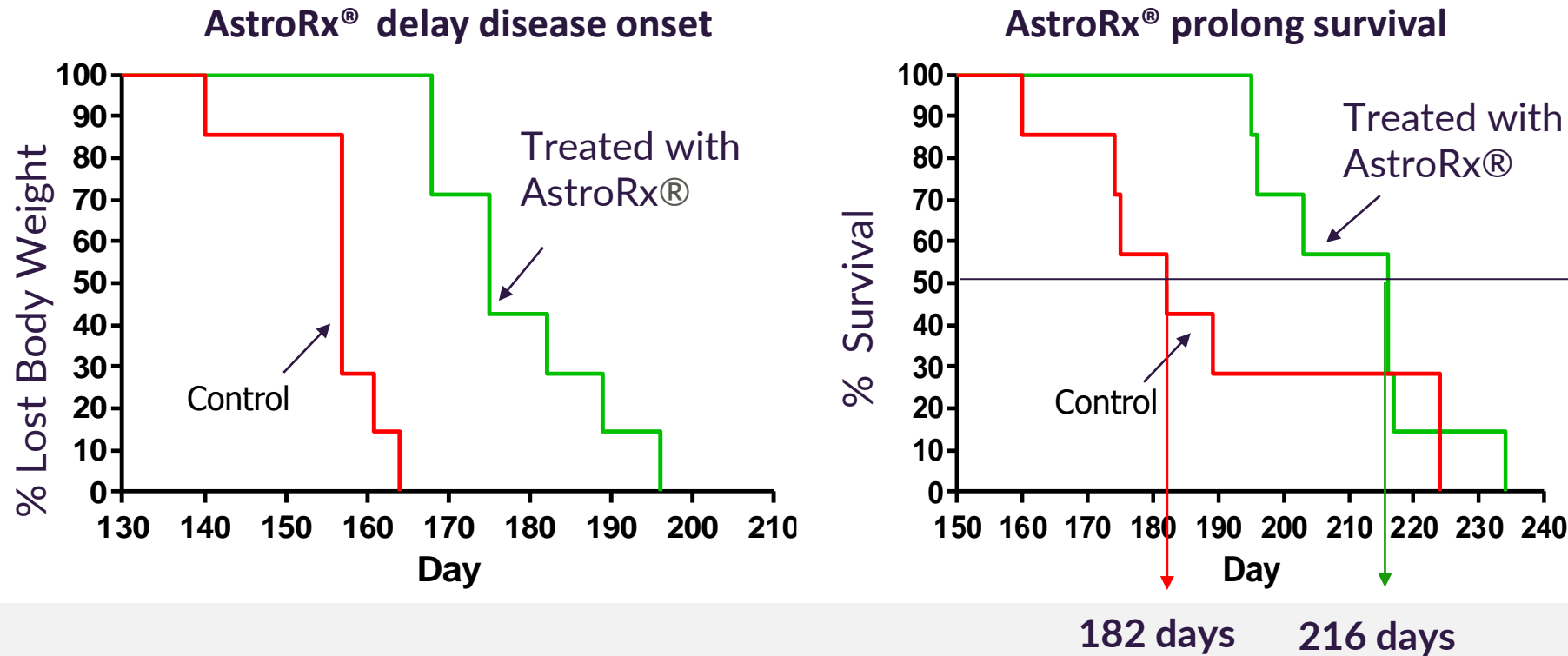
AstroRx® cells were injected at day 50 and 70 of life

Intrathecal injection of AstroRx®
(Lumbar puncture) between L5-L6
w/o immunosuppression



hSOD1G93A high copy number rat (ALS model)

AstroRx[®] Prolong Survival of hSOD1 Rats



- Significant delay in disease onset in AstroRx[®] treated rats (P=0.0001)
- Prolonged survival in AstroRx[®] treated rats

AstroRx[®] Mechanism of Action

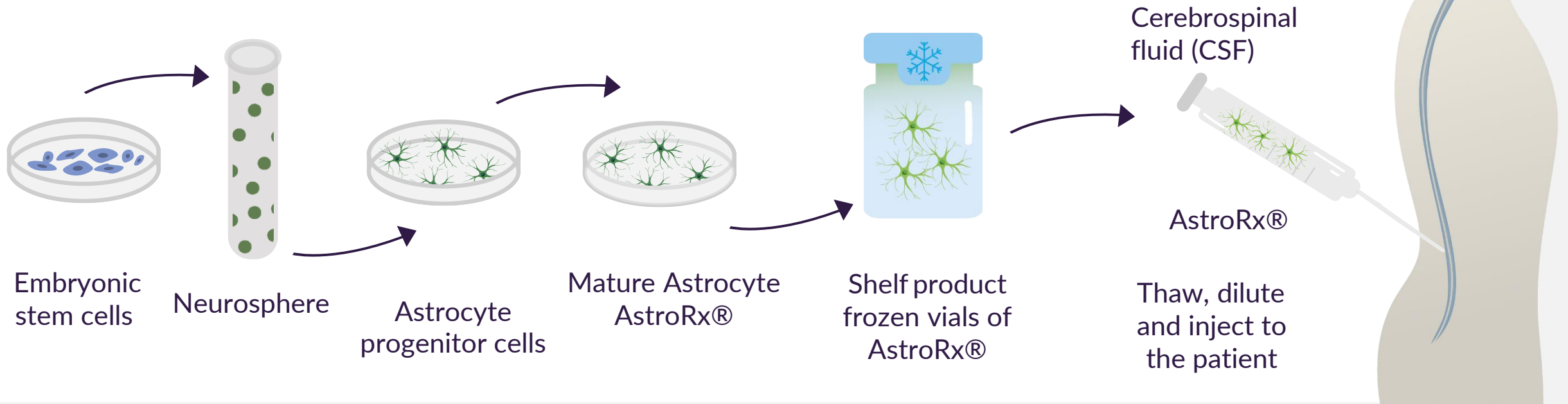




First In Human Clinical Trials Using AstroRx®

Cell Therapy Using AstroRx® - The Process

Production of human astrocytes from ES cells stored frozen for intrathecal injections



AstroRx[®] Phase 1/2a Status

Good Clinical Safety Profile

Study Status:

- 5 patients in Cohort A and 5 patients in Cohort B completed 12 Month follow up.
- Cohorts C&D were discontinued following Data Safety Monitoring Board (DSMB) recommendation due to COVID-19 pandemic

Safety Results:

- Good safety profile
- No treatment-related serious adverse events
- No dose-limiting toxicities were reported

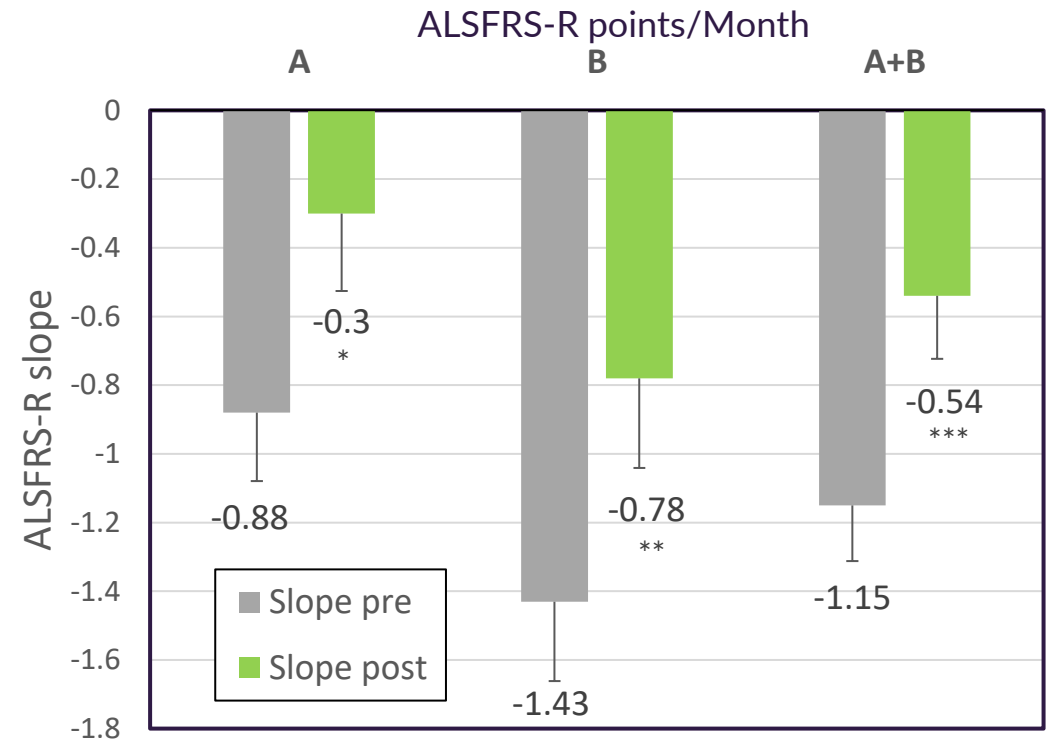


AstroRx[®] 3-month Follow-up Results

Demonstrated a Clinically Meaningful Decline in Disease Progression

Clinical results are consistent between Cohorts A and B

ALSFRS-R slope difference between 3 months pre- and post-treatment in Cohorts A and B



* p=0.0396, **p=0.0023, *** p=0.0004 (MMRM analysis)

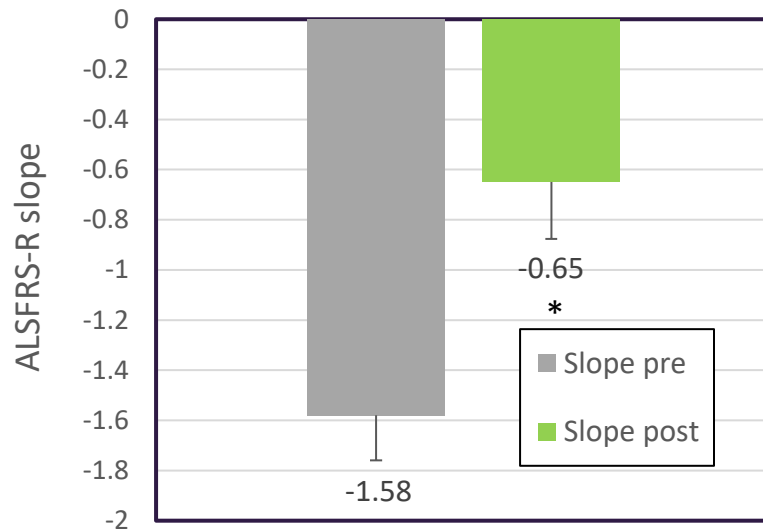
ALSFRS-R is a Clinically Accepted Measure of Disease State

AstroRx[®] Efficacy Among ALS Rapid Progressors (3-month Follow-up)

80% of rapidly progressing patients responded to treatment of AstroRx[®]

ALSFRS-R Slope Analysis

Rapid Progressors (A+B)



* p=0.0003 (MMRM analysis)

- Rapid progressors are defined as patients who deteriorate at least 1.1 points of ALSFRS-R per month in the run-in period
- Analysis of rapid progressors is particularly important since the inclusion of this sub-population of patients in clinical trials in ALS increases the likelihood of demonstrating a drug effect
- Responders are defined as showing improvement of at least 25% in the ALSFRS-R rate of decline between pre- and post-treatment periods

AstroRx[®] study: 1-year Follow-up Results

The results support our plan for a further clinical trial with repeated intrathecal administrations of AstroRx[®], in order to prolong the clinical effect seen by a single dose

- Safe and well tolerated in both treatment doses over 12-months
- No treatment-related serious adverse events (SAEs) nor dose-limiting toxicities were reported



 AstroRx[®] Continued Safety Results

AstroRx[®] Patent Strategy

- ✓ DIRECTED DIFFERENTIATION OF ASTROCYTES FROM HUMAN PLURIPOTENT STEM CELLS FOR USE IN DRUG SCREENING AND THE TREATMENT OF AMYOTROPHIC LATERAL SCLEROSIS (ALS)

Israel

Japan

Europe

Australia

- ✓ METHODS OF GENERATING GLIAL AND NEURONAL CELLS

Israel

USA

- ✓ METHODS OF GENERATING GLIAL AND NEURONAL CELLS AND USE OF SAME FOR THE TREATMENT OF MEDICAL CONDITIONS OF THE CNS

Europe

USA

Hong Kong

Israel



AstroRx[®] Clinical and Regulatory Plan

- FDA has approved the IND for AstroRx[®] for its planned phase IIa clinical trial
- To commence the phase IIa clinical trial in the USA at multiple sites
- A clinical development strategy to support the product intended use
- A RMAT* designation application is planned, to enable expedited development, reviews and to accelerate approval



IsletRx

Functional Islet Cells - Potential Cure for Insulin Dependent Diabetes

IsletRx Cell
Product



Insulin Dependent Diabetes - Market and Facts



537 million adults are living with diabetes worldwide – 1 in 10*



Highly demanding disease management. Insulin injection treatment does not prevent long term complications**



In 2022, there were 8.75 million people living with type 1 diabetes globally. 1.52 million of these people were under 20 years old***



Diabetes was responsible for an estimated USD 966 billion in global health expenditure in 2021. This represents a 316% increase over the last 15 years*

Unmet Need in Insulin Dependent Diabetes



Insulin Therapy and glucose management are not a cure

Even with strict insulin treatment regimens, patients experience:

- Frequent episodes of severe, undetected hypoglycemia;
- Severe glycemic lability
- Progressive diabetic complications:
 - Neuropathies
 - Heart Disease
 - Retinopathy
 - Kidney failure
 - Stroke

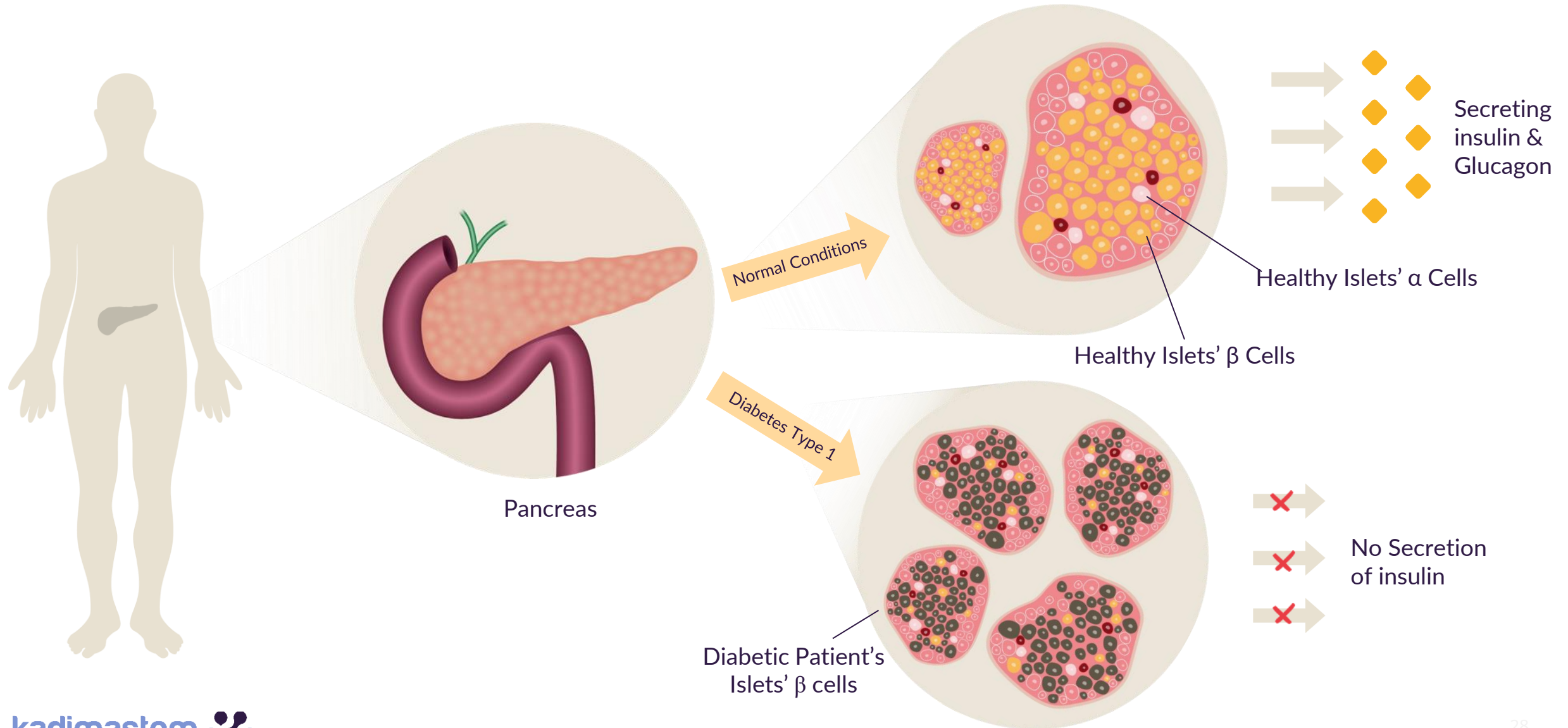


Islet Transplantation

Restoring patient's ability to naturally produce insulin

- Healthy and functional islet cells can produce and secrete insulin in a regulated manner
- Cadaveric donor islet cell therapy is a safe and clinically validated treatment for Insulin-Dependent Diabetes*
- Patients treated achieved Insulin independence for ~2 years following treatment**
- Main challenges remaining: ***a severe shortage of donor islet cells and immune suppression that is unhealthy and not always prevent immune rejection***

What Happens in Diabetes Type 1





Cure for Insulin Dependent Diabetes using **IsletRx**

Our Treatment = Cure

Problem

Our Treatment

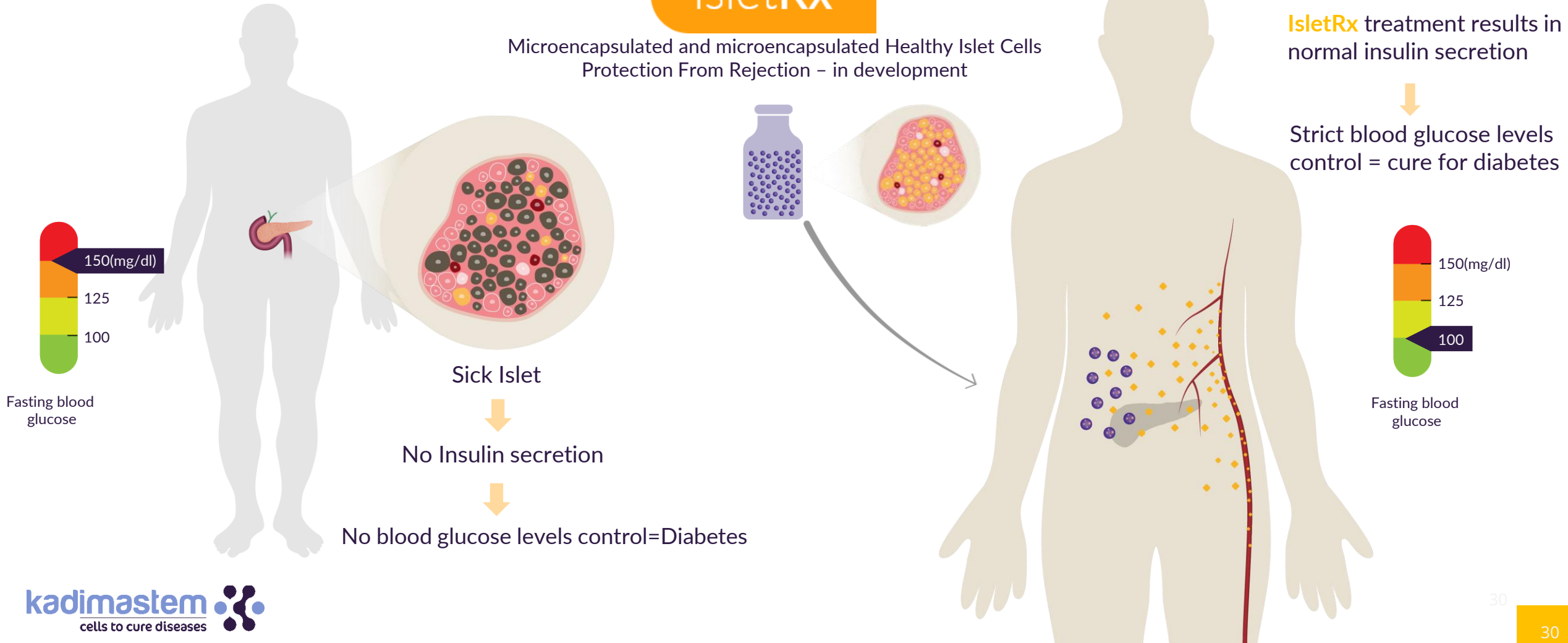
Cure

IsletRx

Microencapsulated and microencapsulated Healthy Islet Cells
Protection From Rejection – in development

IsletRx treatment results in
normal insulin secretion

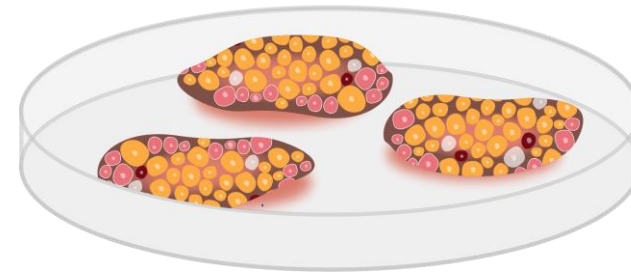
Strict blood glucose levels
control = cure for diabetes



IsletRx - Our Solution

Functional pancreatic islets derived from hES cells that produce and secrete insulin and glucagon glucose dependently

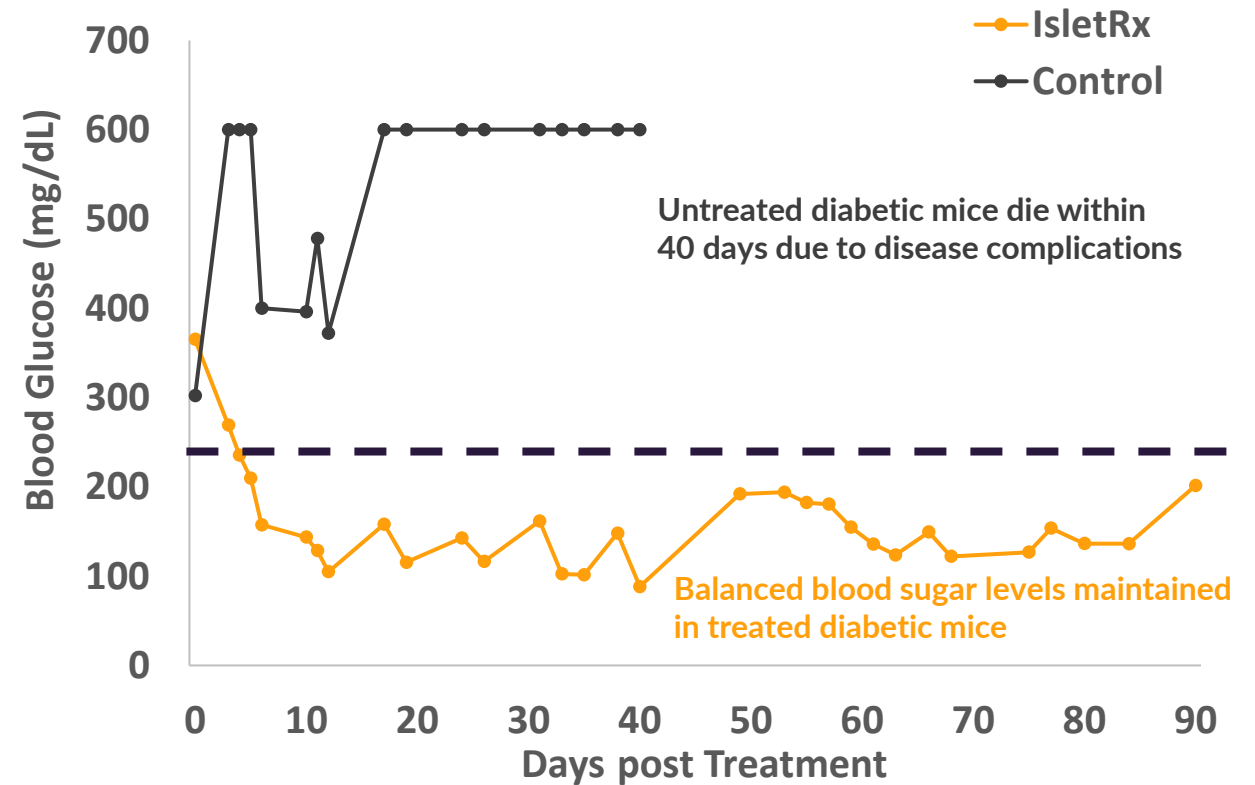
- Overcome donor tissue availability shortage
- Replace malfunctioning patient islet cells
- Maintain continuous balanced glucose levels
- Show long term functionality, protected from host immune response, **without immune suppression drugs** - in development



IsletRx - Preclinical Demonstration of Efficacy

IsletRx treated diabetic mice (STZ) demonstrated balanced and normal blood glucose levels

- Long-term therapeutic effect was achieved in an **immunocompetent animal model** (C57BL/6 mice)
- IsletRx cells well protected from host immune system



IsletRx - Production, Selection and Encapsulation

Large Scale Production:

Scalable 3D bioreactor production

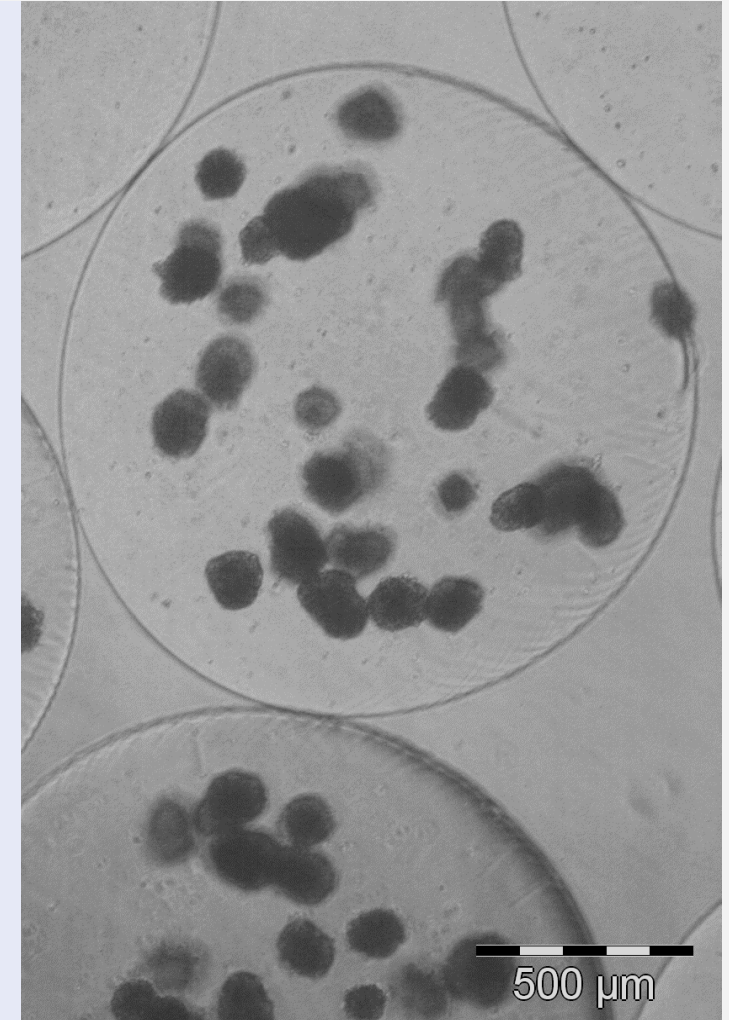
Selection & Enrichment:

Proprietary technology (IP) enables islet cell enrichment and selection, achieving well characterized cell identity

- Novel CD26-/CD49a+ signature cell surface markers are used to identify and select highly functional insulin producing cells, thereby increasing the probability of clinical efficacy

Unique Microencapsulation Technology:

Demonstrate positive results in protecting IsletRx cells from host immune system response, overcoming a major challenge in allogeneic cell therapy. Other macroencapsulation technologies are tested concomitantly.



Microencapsulated ILCs - IsletRx

IsletRx Potential Advantages vs. Available Treatments

	IsletRx Allogeneic Islet Transplantation	Insulin Injections	Insulin Pumps
Periodic Treatments, Long-term Effect	✓	✗ Daily injection	✗ Ongoing
Balanced Glucose Levels	✓	✗/✓ Manual monitoring and balancing of glucose levels	✗/✓ Delay in real-time glucose measurement and insulin infusion
Personal Comfort	✓	✗ Daily routine interference- injections and laborious monitoring	✗ External device necessitating maintenance
Compliance	✓	✗ Requires high-level treatment management	✗ External device necessitating maintenance
Prevention of Long-term Complications	✓	✗	✗

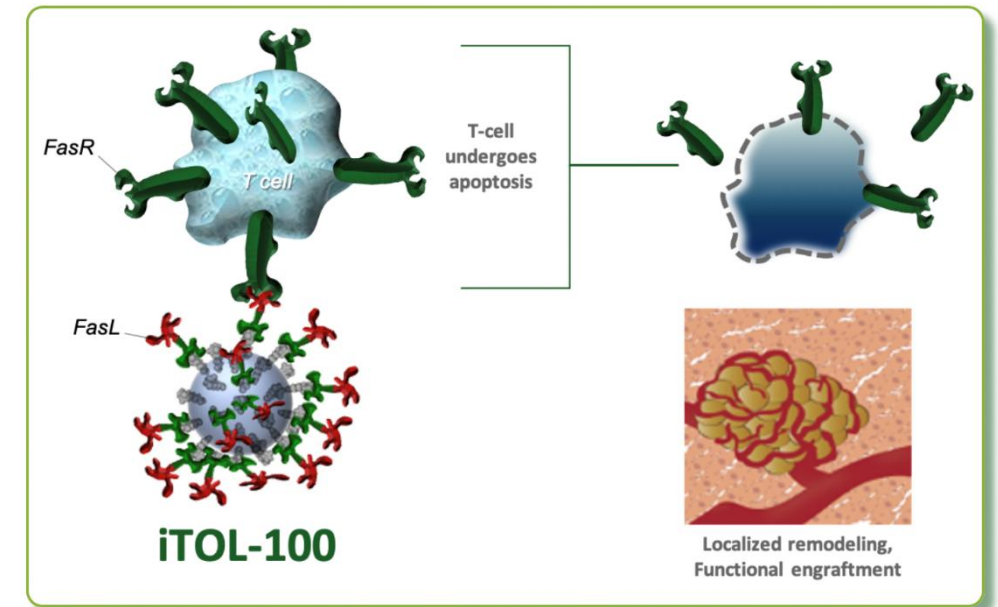
IsletRx – iTolerance

Local Immune Suppression

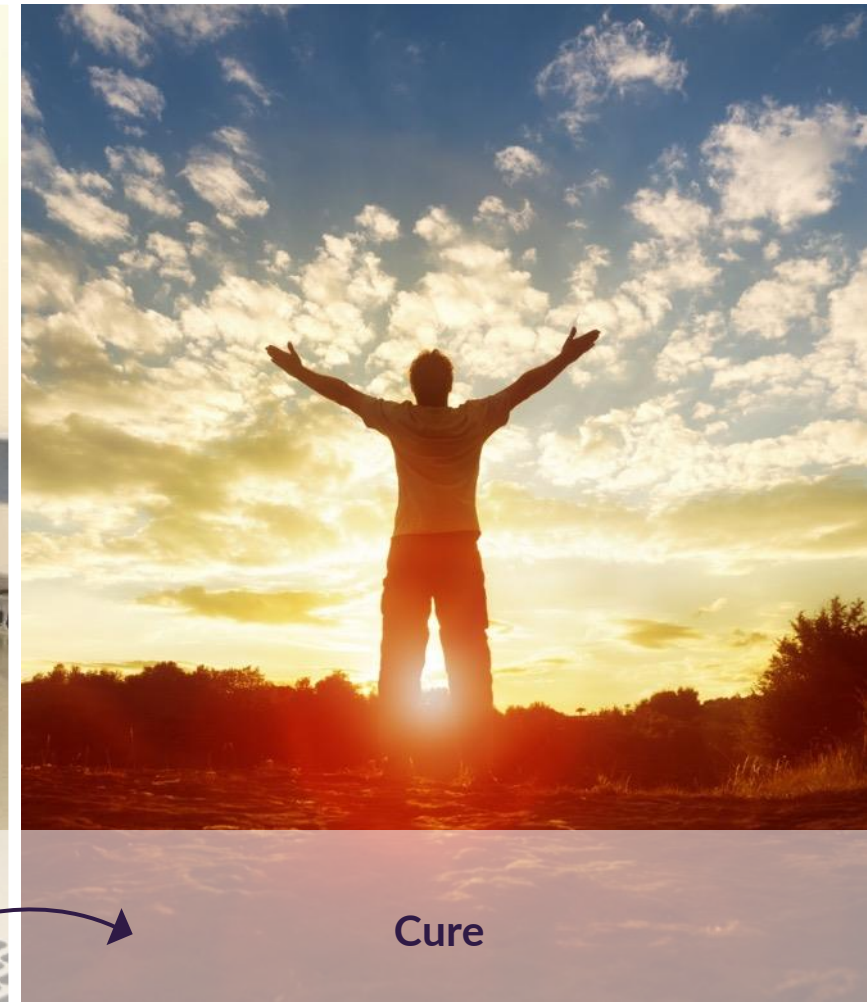


iTOLERANCE

- Regenerative medicine without the need for life-long immunosuppression
- Leverages the naturally occurring protein, Fas Ligand (FasL)
- Creating localized immune privilege
- BIRD Grant – Submitted
- INTERACT Meeting with the FDA (January 2024)



Our Treatment = Cure



IsletRx Patent Strategy

✓ INSULIN PRODUCING CELLS DERIVED FROM PLURIPOTENT STEM CELLS

Israel

Europe

USA

Australia

Canada

✓ METHODS FOR DIFFERENTIATING AND PURIFYING PANCREATIC ENDOCRINE CELLS

Israel

Europe

India

USA

Japan



IsletRx Next Steps

- Expand Collaboration
- Pre-IND meetings with FDA
- Upscaling and GMP production
- IND for Clinical Trial



Leadership Team



Ronen Twito CPA

Executive Chairman & President

Over 20 years of financial and managerial experience, including executive positions in NASDAQ and TASE listed companies, leading multiple IPOs and follow-on offerings on Nasdaq, as well as M&As in biotechnology.



Prof. Michel Revel

Founder, Director & CSO

Developed Merck's blockbuster multiple sclerosis drug REBIF® (\$1.7 billion in US sales in 2016) and has over 40 years of experience in biotechnology, genetics, virology and CGT.



Michal Izrael, PhD

VP R&D



Asaf Shiloni

CEO

Over 20 years of experience in the biotechnology industry, Sold PeproTech to Thermo Fisher in 2021 for \$1.85 billion.



Kfir Molakandov, PhD

Director of Diabetes Research and Innovation

Thank You.



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