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cells to cure diseases

Cell Therapies that cure

November 2024 (TASE: KDST)

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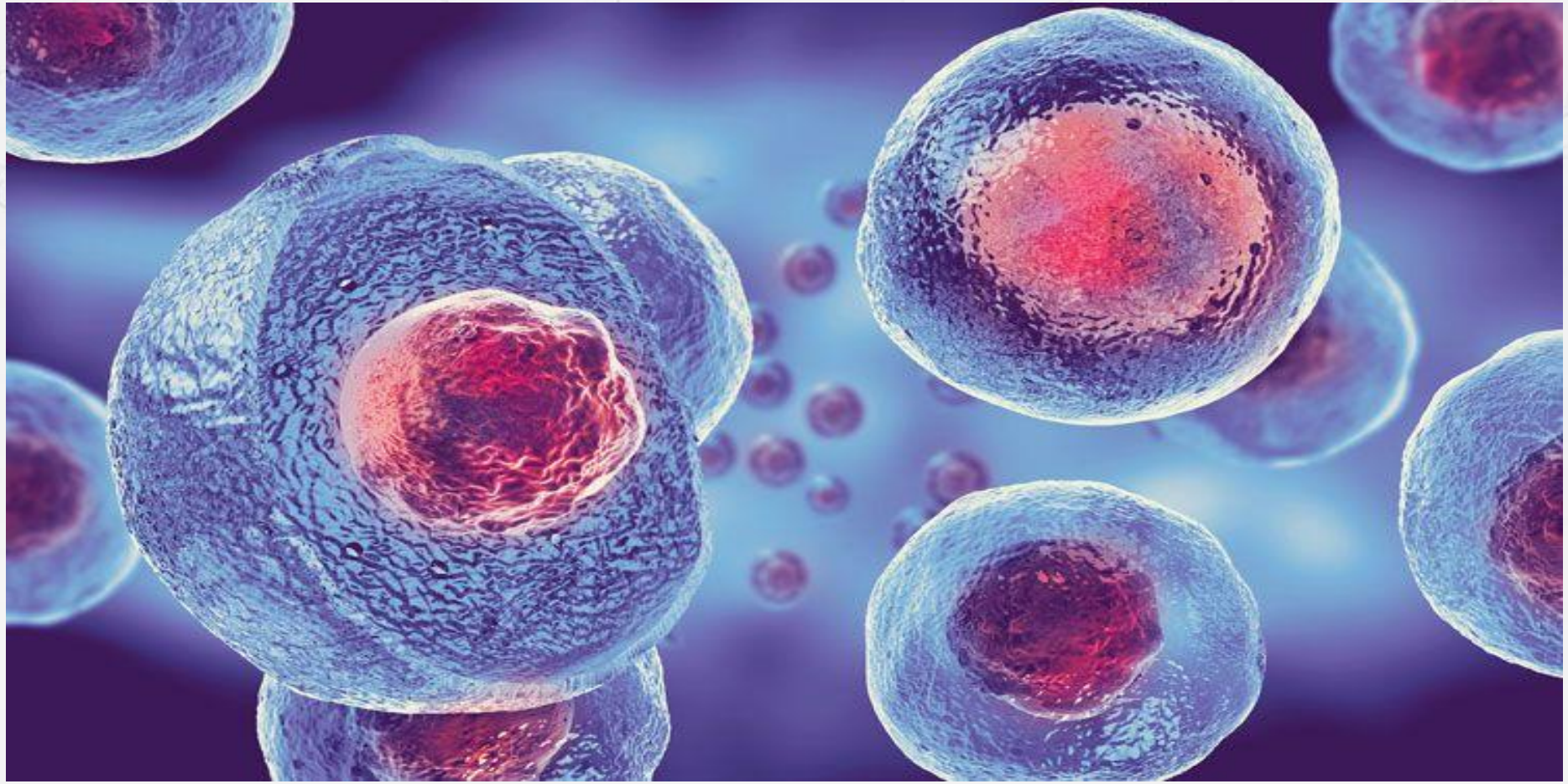
Kadimastem – Stem Cell Derived Cell Therapy



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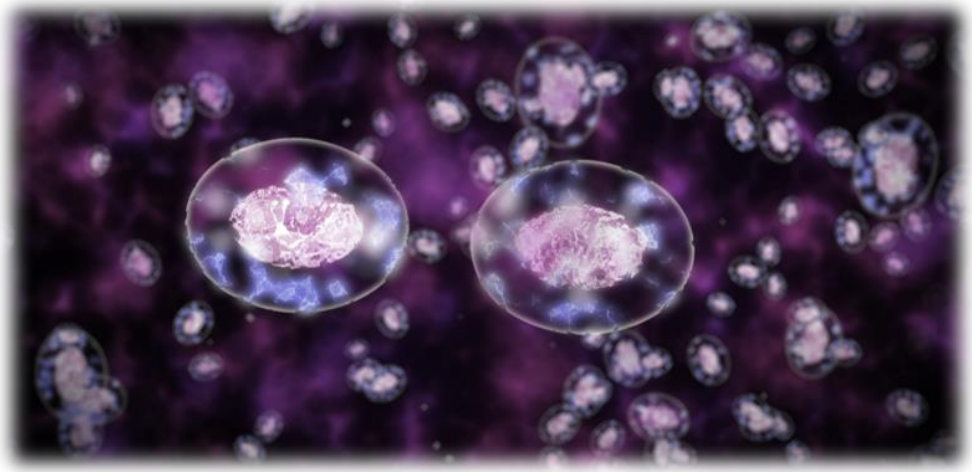
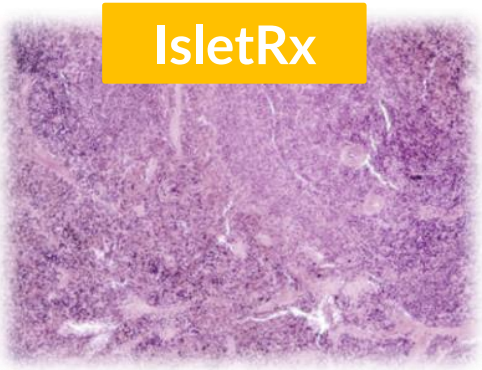
Vision – Stem Cell Derived Cell Therapy

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





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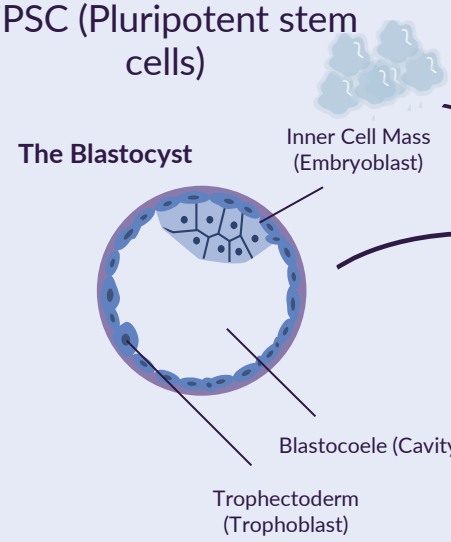
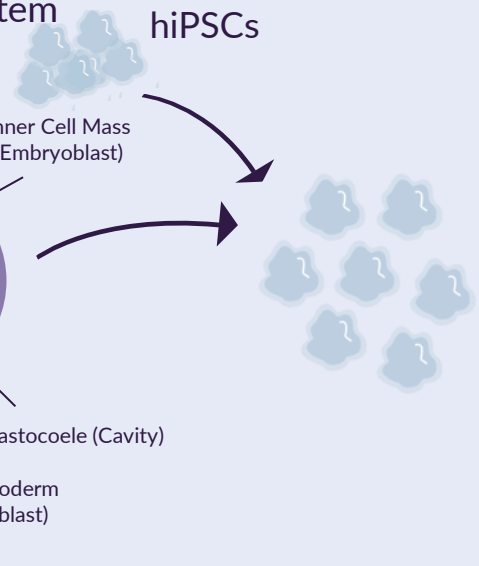
Proprietary Innovative Platform

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

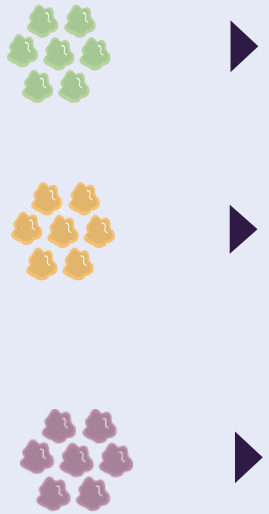
Starting material
clinical grade human embryonic stem cells or hiPSC (Pluripotent stem cells)



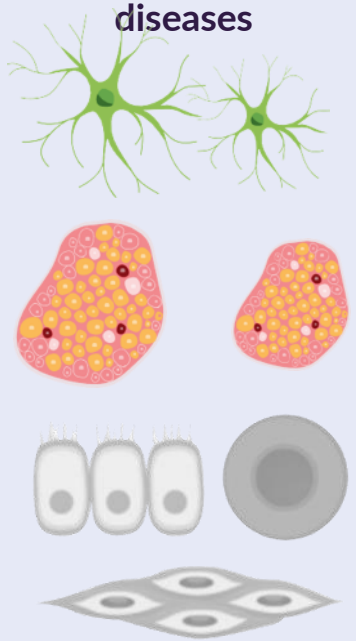
Expansion
Expand indefinitely



Differentiation
Committed progenitor cells



Mature and functional target cells
treatment of a wide range of diseases



Cell product	Indication	
AstroRx®	ALS	Clinical Stage
	Additional neurological indication	
IsletRx	Insulin dependent diabetes	Pre-clinical Stage

Technology platform to allow for differentiation into different cell types

Product Platform Pipeline

CLINICAL

	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	Market

AstroRx® cell Product

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

IsletRx Cell Product

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

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An Active Market – Key Recent Transactions

2019

August 2019

BlueRock

Neurology (Parkinson)
Preclinical stage

Acquisition by Bayer

$600M.

2019

September 2019

Semma Therapeutics

Diabetes
Preclinical stage

Acquisition by Vertex

$950M.

2020 (Covid-19)

2021

February 2021

Sana Biotechnology, Inc.

Regenerative Cell Technology
Preclinical stage

IPO – Nasdaq

$6.38B Market Cap

Morgan Stanley · Goldman Sachs · JPMorgan Chase & Co. · BofA SECURITIES

2022

January 2022

Amylyx

ALS Drug

IPO – Nasdaq

Raised $190 Million at Pre-money evaluation of $1B

2022

July 2022

ViaCyte

Regenerative Cell Technology
Diabetes
Preclinical stage

Acquisition by Vertex

$320M.

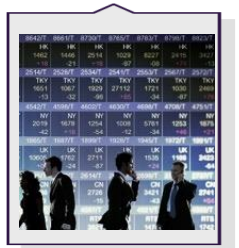
To the best of Company's knowledge, base on the following:

- 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://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

Kadimastem: History & Way Forward

2009 — Company Founding

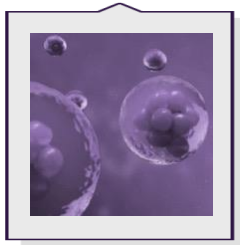
2013 — IPO - TASE



2015 — Pre-IND meeting with FDA for AstroRx

Development of IsletRx from ESCs

2017 — Developing Microencapsulation Technology for IsletRx



2019 — Develop Frozen AstroRx® product

Pre-Clinical success IsletRx

2020 — **Commencing phase 1-2a clinical trials for ALS**

2021 — INTERACT Meeting with FDA for IsletRx (Diabetes)

New Management New Directors taking Kadimastem forward

2023 — **FDA approval of IND submission for Phase IIa clinical trial (ALS)**

IND AstroRx

FDA

Collaboration with iTolerance for Diabetes BIRD funding

iTOLERANCE

BIRD

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2024

REVERSE MERGER

Nasdaq

Pre-IND IsletRx

Diabetes

2025

ALS US Clinical Trial

FDA

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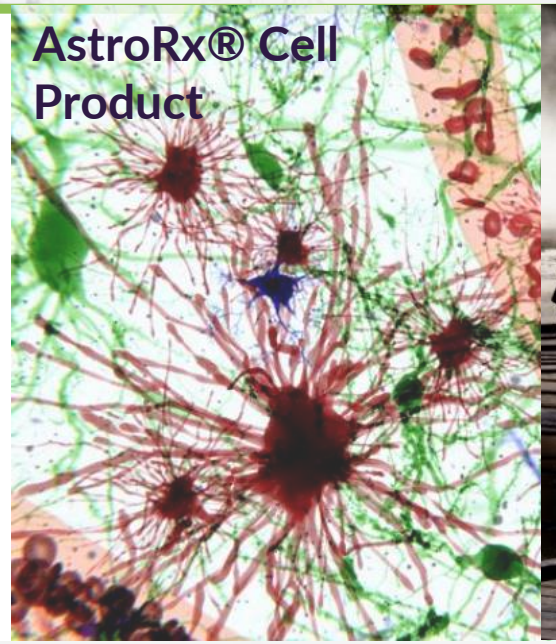
AstroRx ®

Astrocytes- Cell Therapy Treatment for Neurodegenerative Diseases



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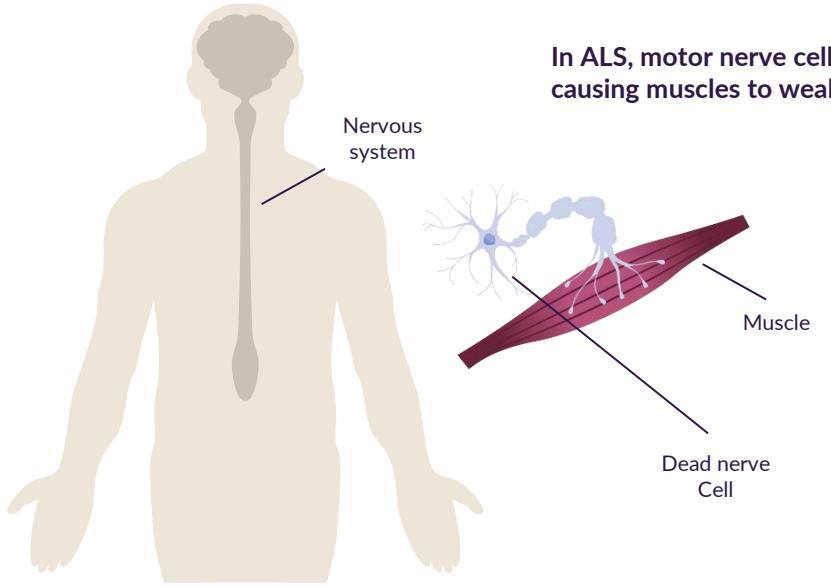
ALS– Market and Facts

- 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 **450,000**[1] ALS patients estimated worldwide, **30,000** patients in the US[2]
- **Global ALS treatment market valued at US$300 million in 2023**[3]

  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 M[3]
- **US ALS Healthcare costs:**

  Close to $1.02 billion annually direct and indirect associated costs[4].

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

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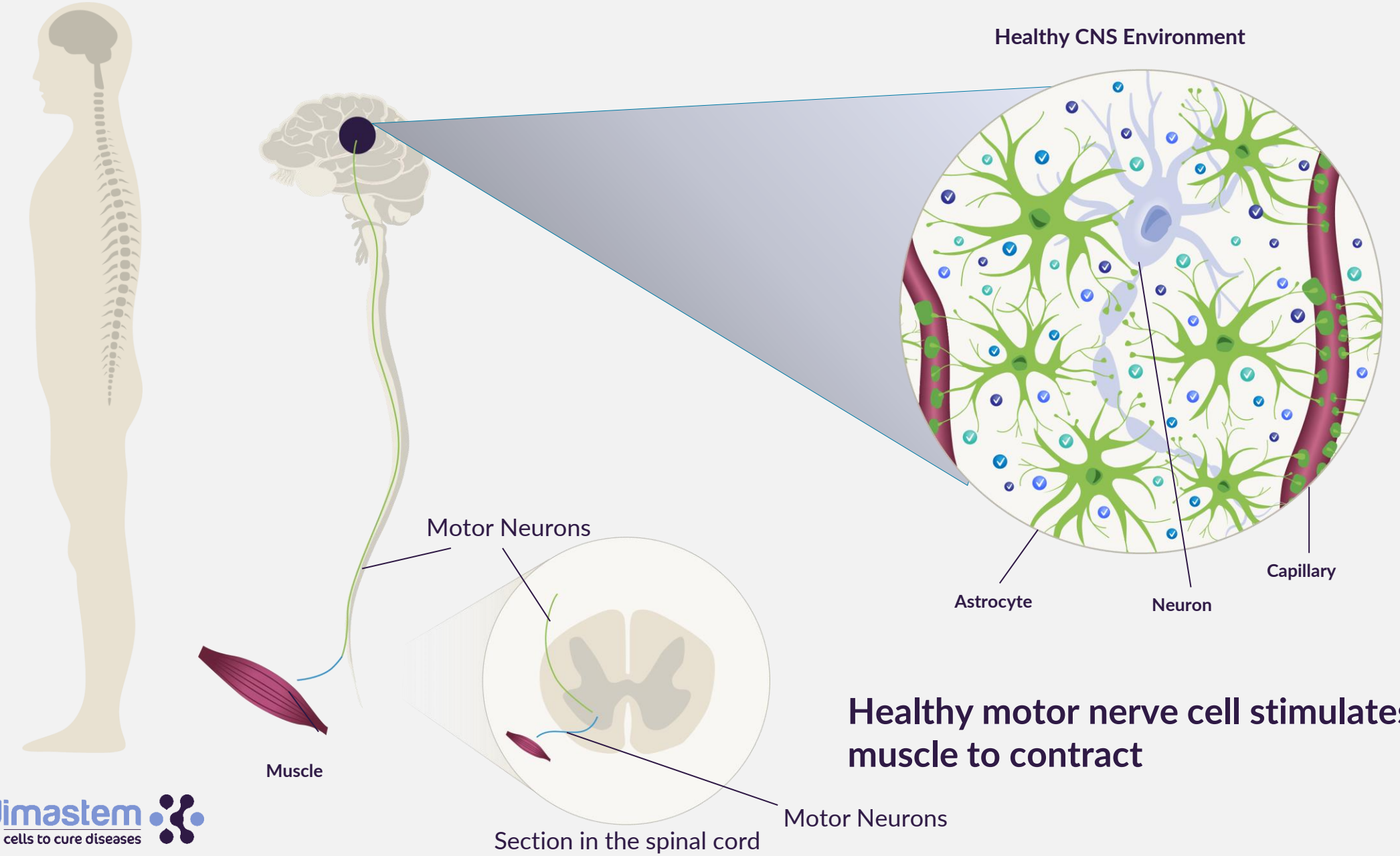
The Central Nervous System



Healthy motor nerve cell stimulates muscle to contract

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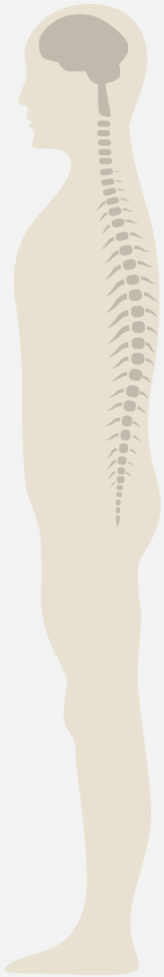
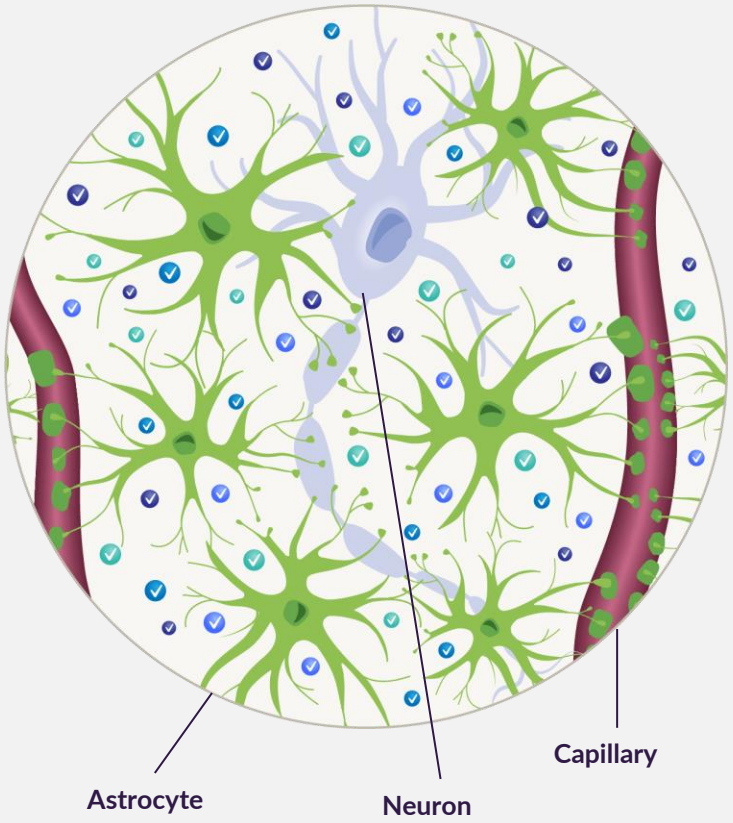
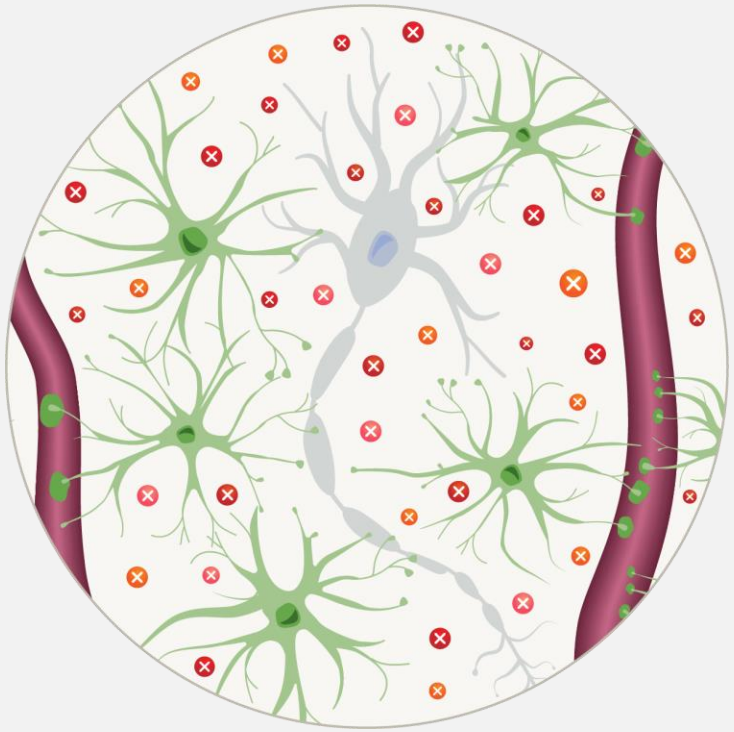
Use Astrocytes for ALS - AstroRx®



Healthy CNS Environment

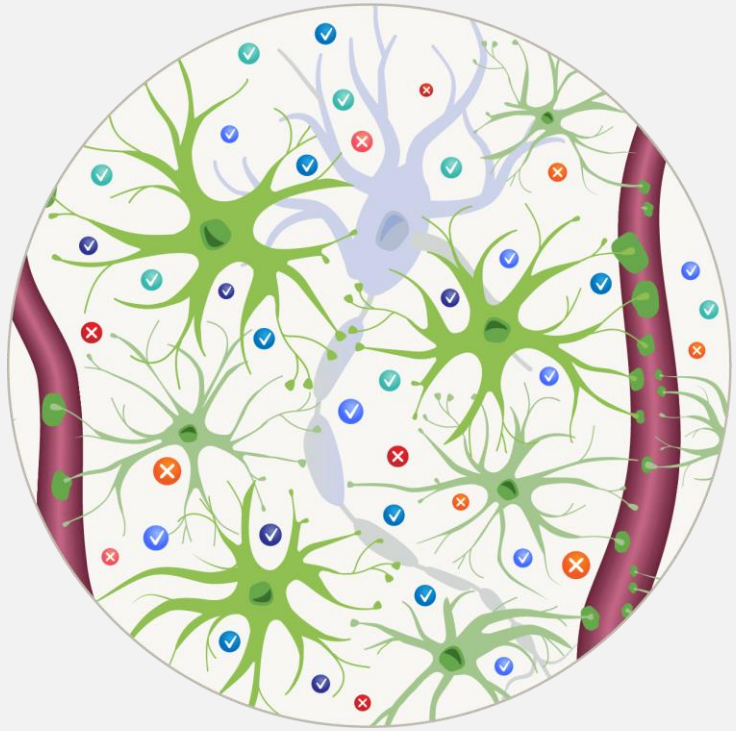


ALS Patients' CNS Environment



Astrocytes malfunction in ALS

Injecting AstroRx®
Healthy, Functional Astrocytes in the CNS



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

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Why Use Astrocytes for ALS - AstroRx®

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

	Mechanism of Action	ALS Patients' Astrocytes	AstroRx® Healthy, Functional Astrocytes
In ALS, the patient's own astrocytes fail to support motor neuron survival	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)

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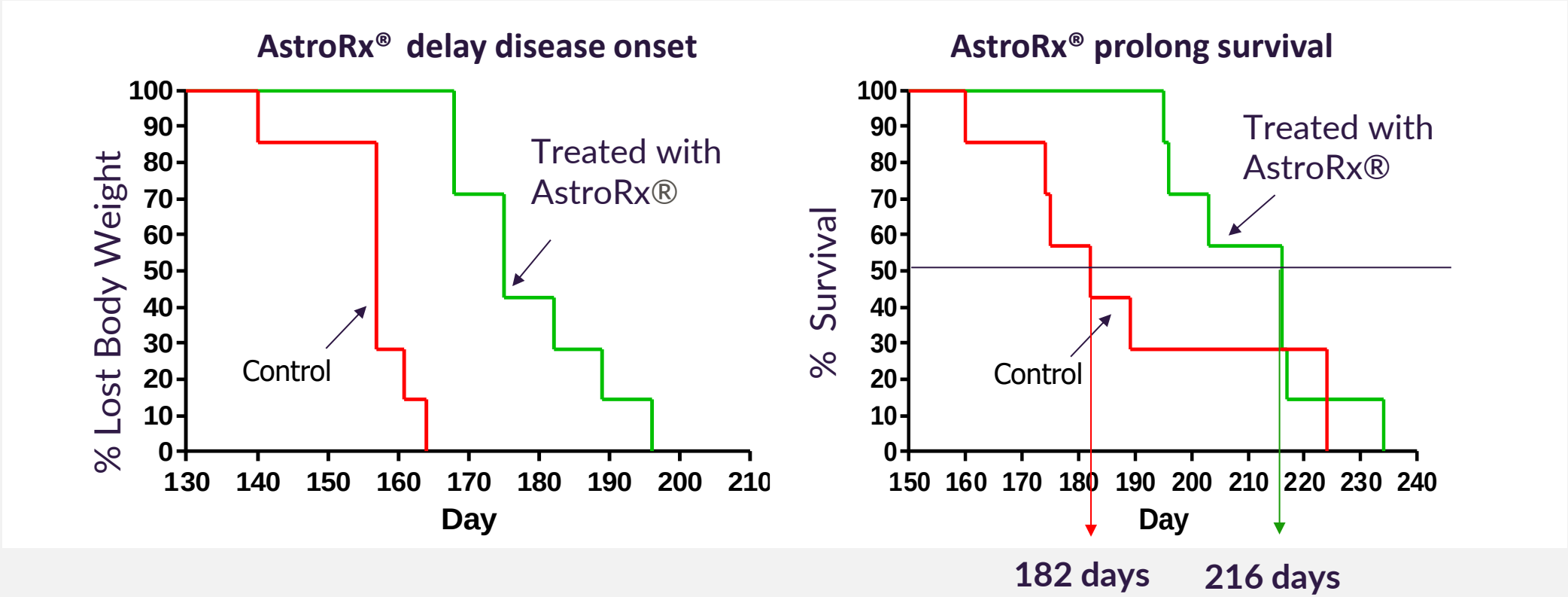
AstroRx® Prolong Survival of hSOD1 Rats



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

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AstroRx® Mechanism of Action

First In Human Clinical Trials Using AstroRx®

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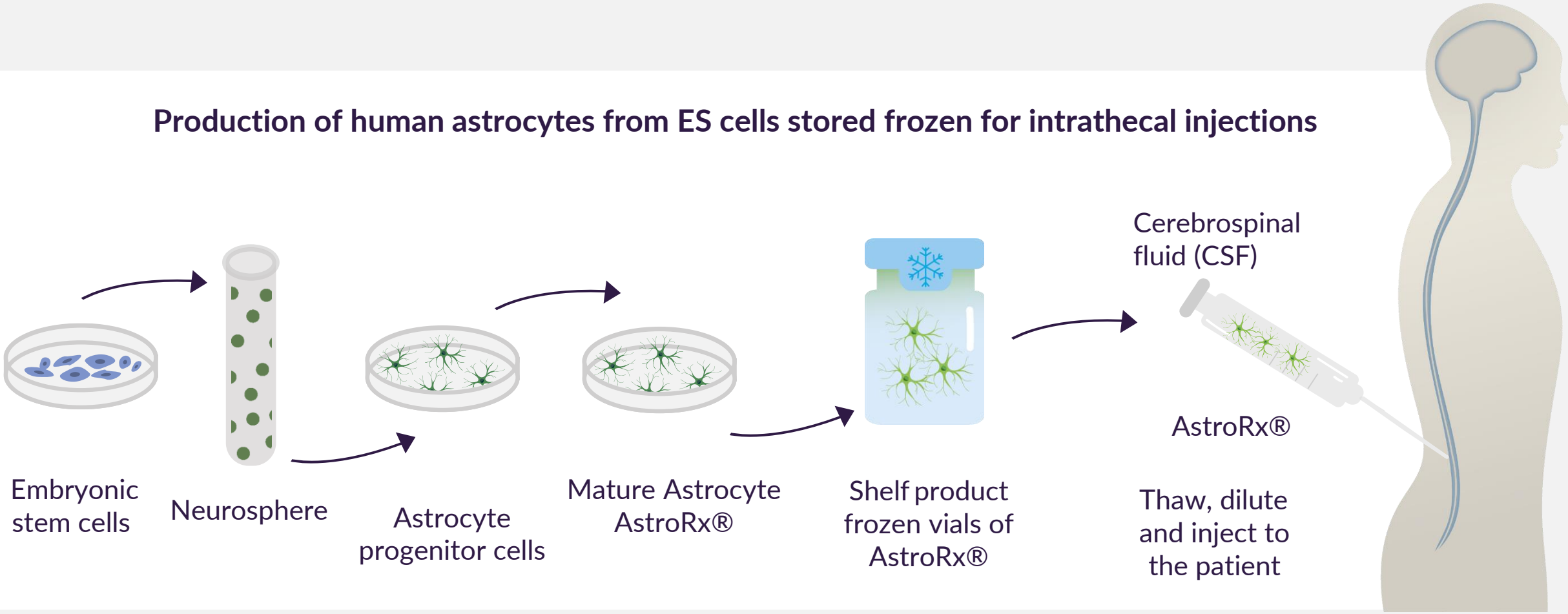
Cell Therapy Using AstroRx® - The Process

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



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AstroRx® Phase 1/2a Status

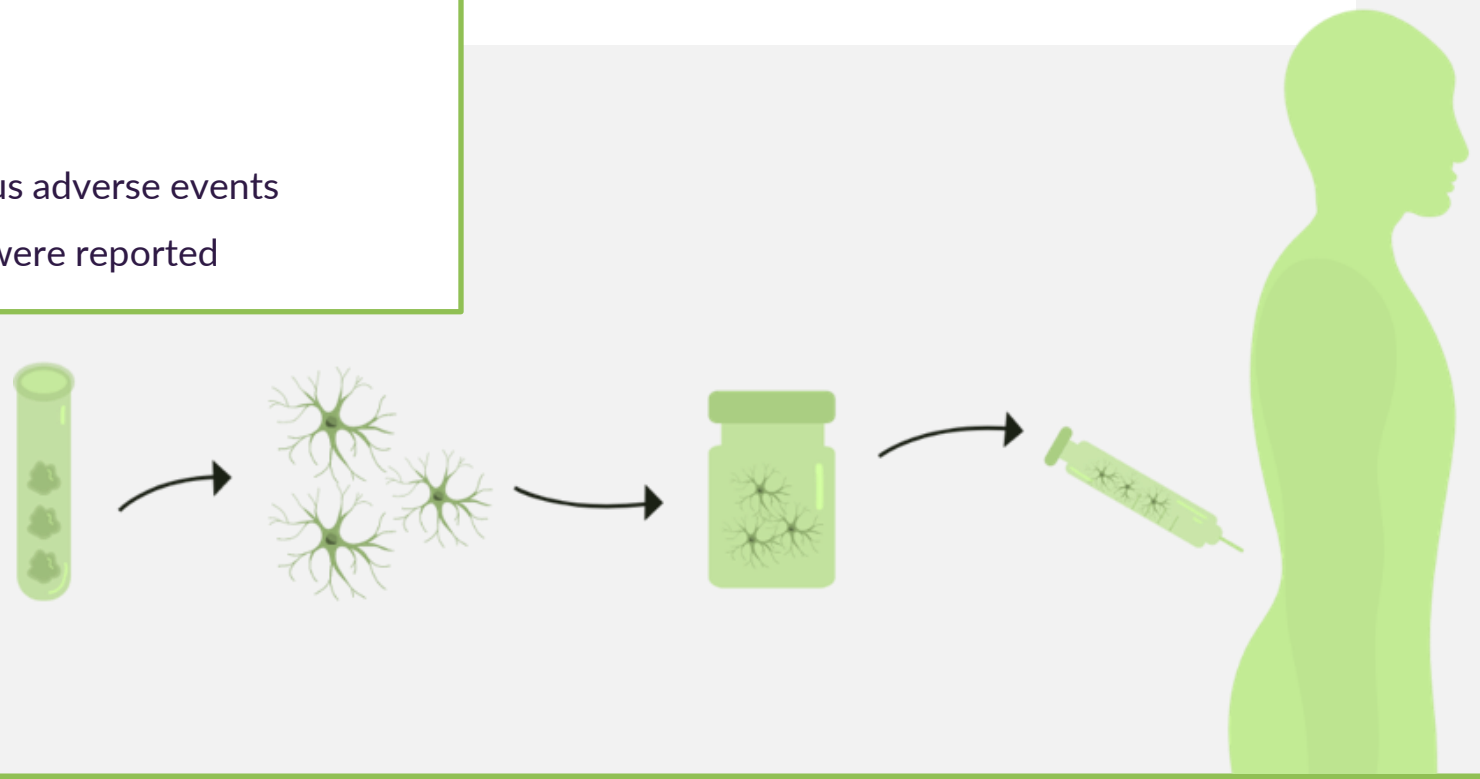
Good Clinical Safety Profile

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



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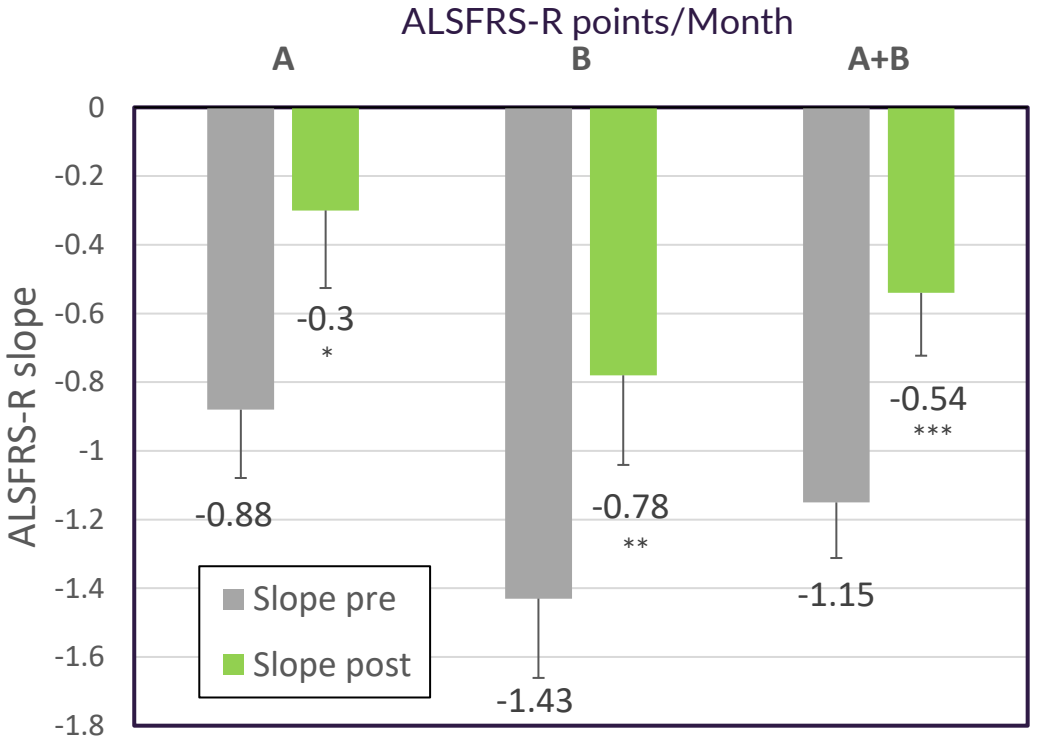
AstroRx® 3-month Follow-up Results

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

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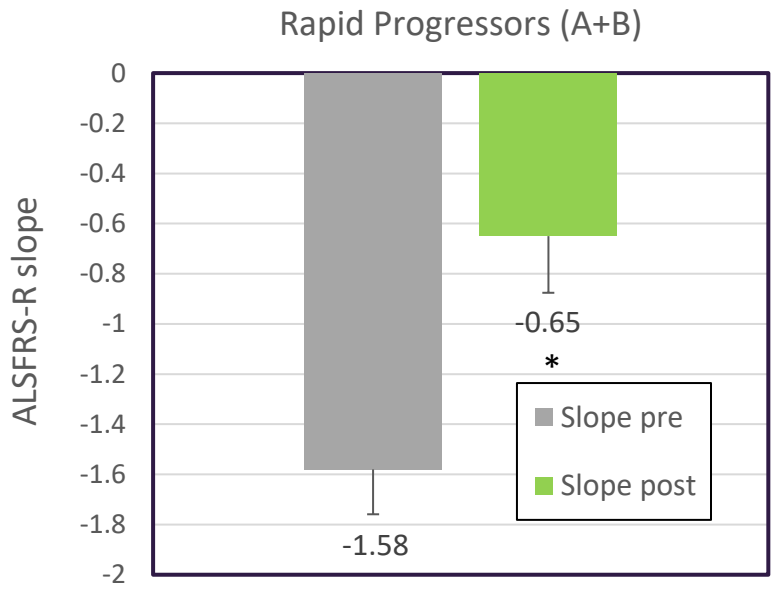
AstroRx® Efficacy Among ALS Rapid Progressors (3-month Follow-up)

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

ALSFRS-R Slope Analysis



* 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

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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

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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®

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AstroRx® Clinical and Regulatory Plan

- FDA has approved the IND for AstroRx® for its planned phase IIa clinical trail
- 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

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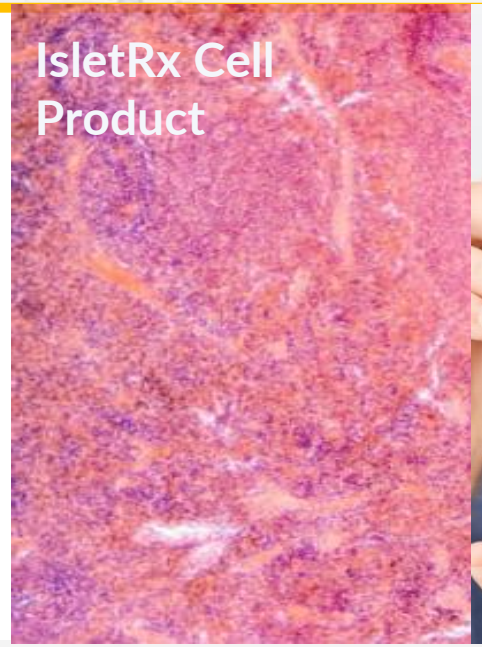
*RMAT - Regenerative Medicine Advanced Therapy

IsletRx

Functional Islet Cells - Potential Cure for Insulin Dependent Diabetes



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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*

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*https://diabetesatlas.org/idfawp/resource-files/2021/11/IDFDA10-global-fact-sheet.pdf
**Tao et al 2010, PLoS One. 2010; 5(7): e11501. doi: 10.1371/journal.pone.0011501
***Type 1 diabetes estimates in children and adults | IDF Diabetes Atlas

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***

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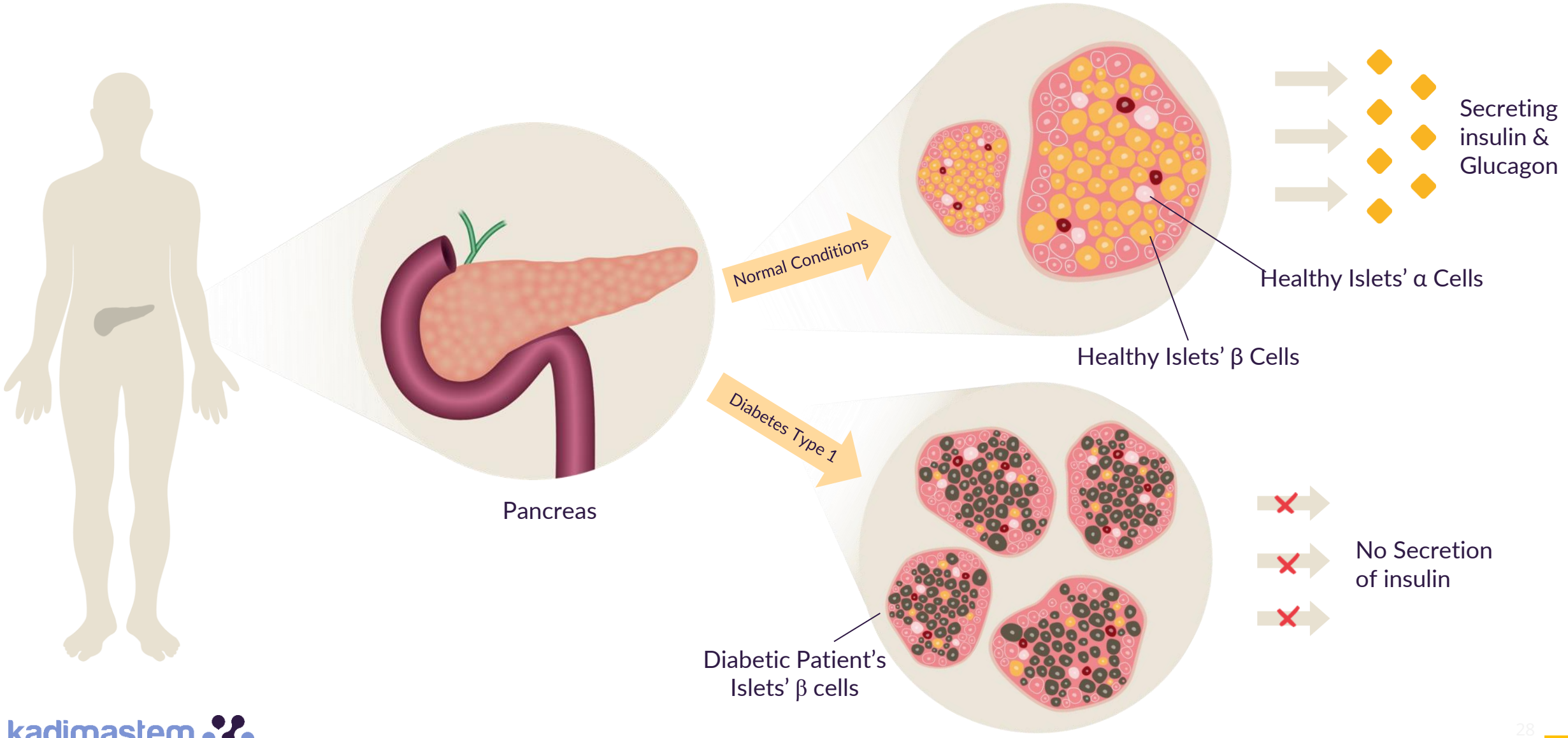
* Shapiro et al 2000
** Bernhard J. Hering 2016
*** https://doi.org/10.1016/B978-0-12-809880-6.00056-4

What Happens in Diabetes Type 1



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Cure for Insulin Dependent Diabetes using IsletRx

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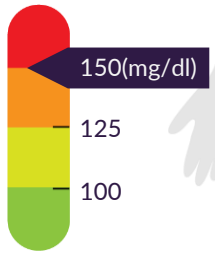
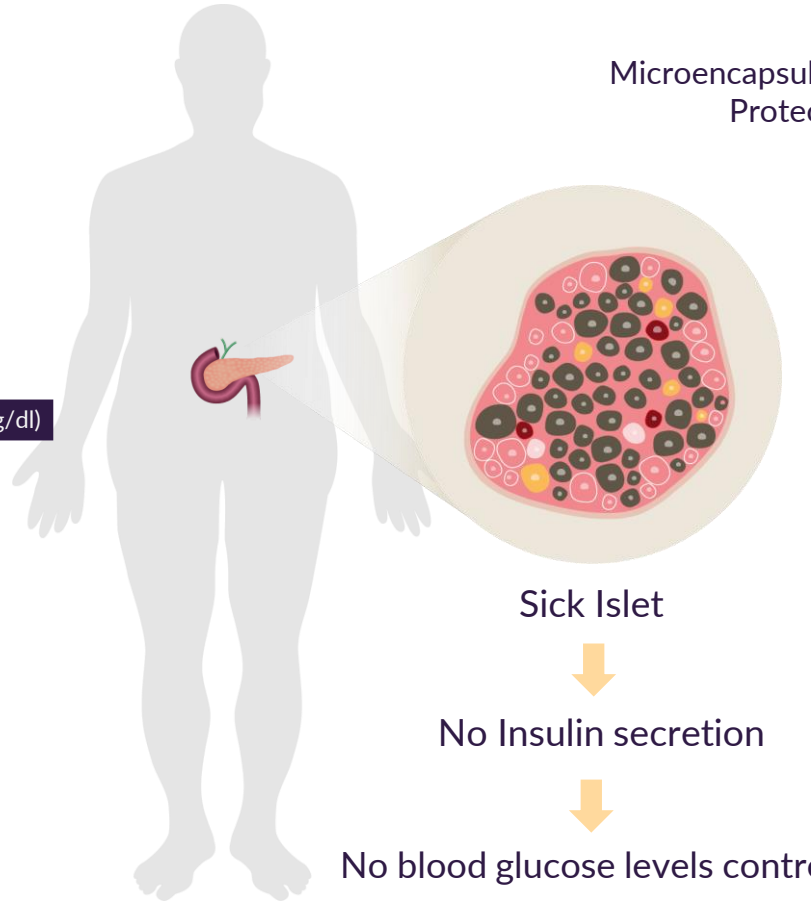
Our Treatment = Cure

Problem



Fasting blood glucose



Sick Islet

↓

No Insulin secretion

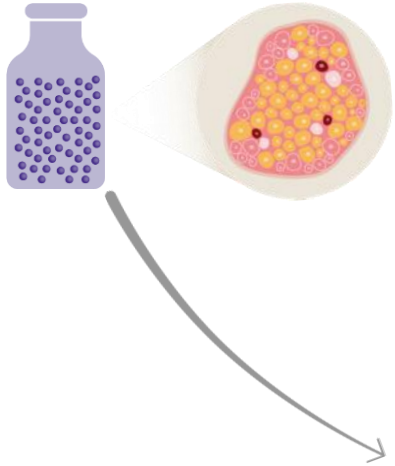
↓

No blood glucose levels control=Diabetes

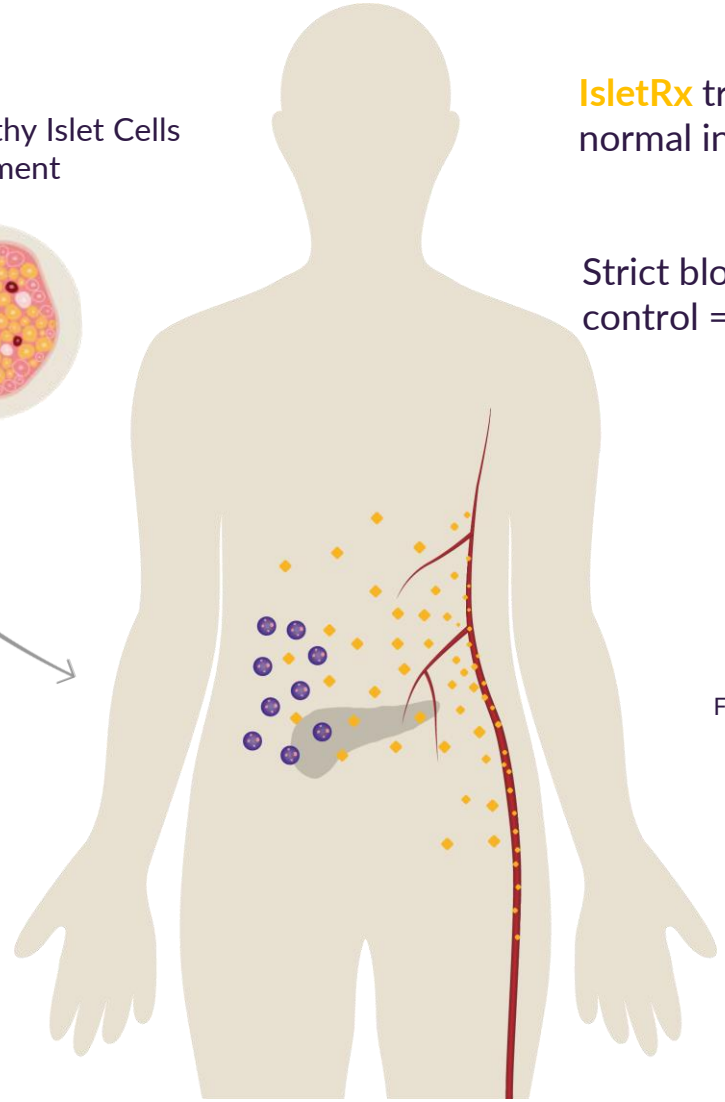
Our Treatment

IsletRx

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



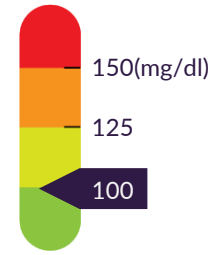
Cure



IsletRx treatment results in normal insulin secretion

↓

Strict blood glucose levels control = cure for diabetes



Fasting blood glucose

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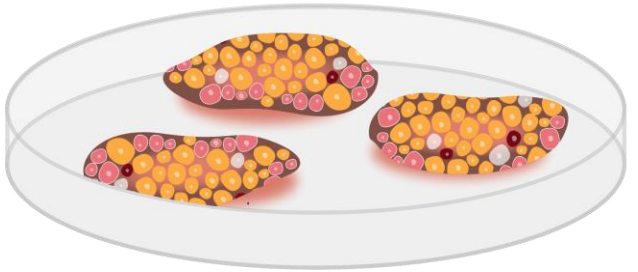
IsletRx - Our Solution

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

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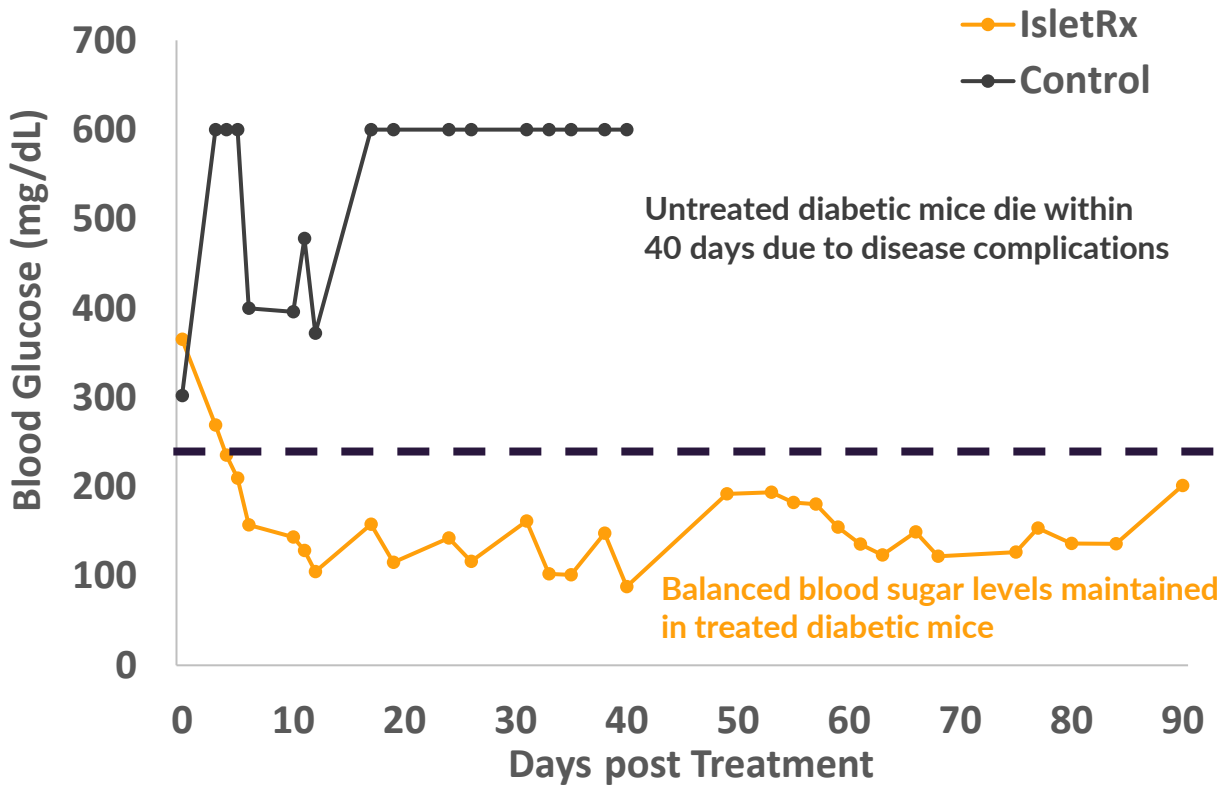
IsletRx - Preclinical Demonstration of Efficacy

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



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Molakandov et al 2021, Frontiers in Endocrinology

IsletRx - Production, Selection and Encapsulation

Large Scale Production:

Scalable 3D bioreactor production

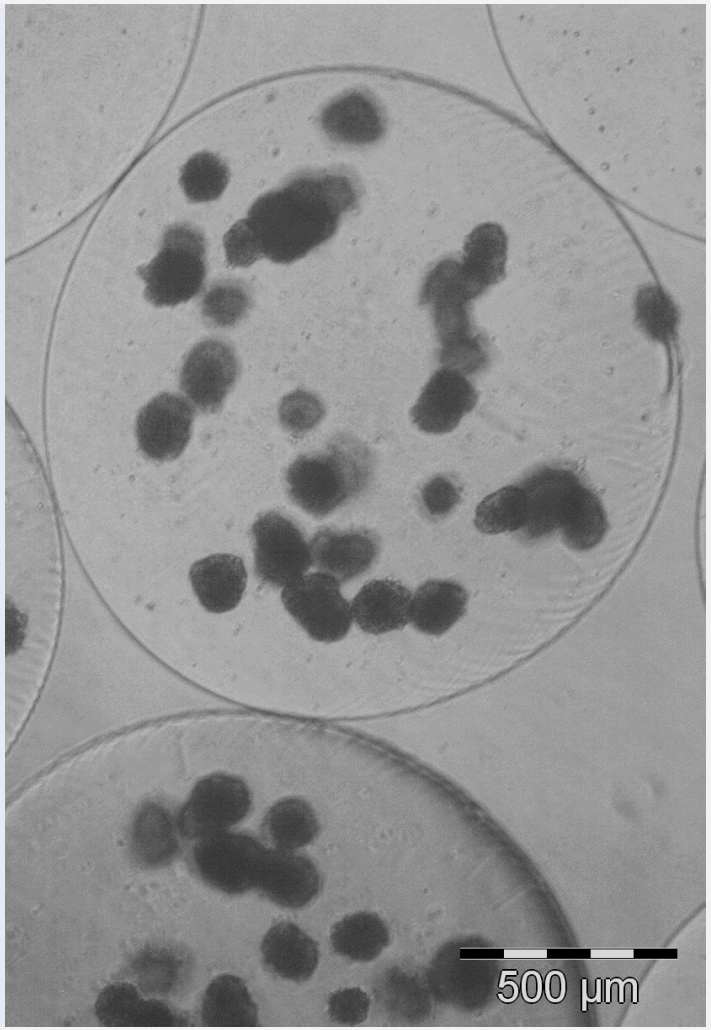
Selection & Enrichment:

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

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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	✓	✗	✗

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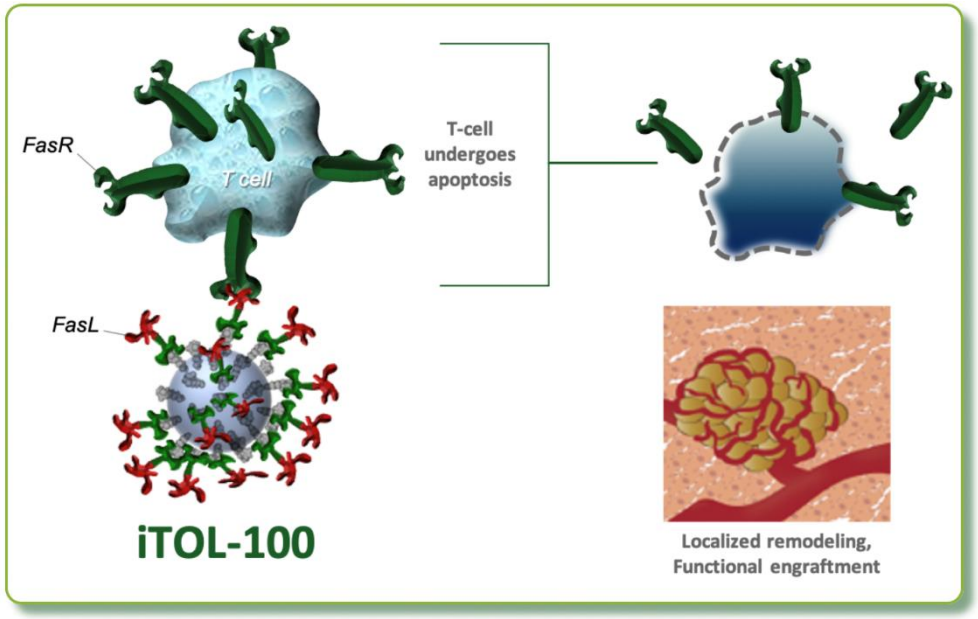
IsletRx – iTolerance

Local Immune Suppression

BIRD
Israel-U.S.
Binational Industrial Research
and Development Foundation

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)



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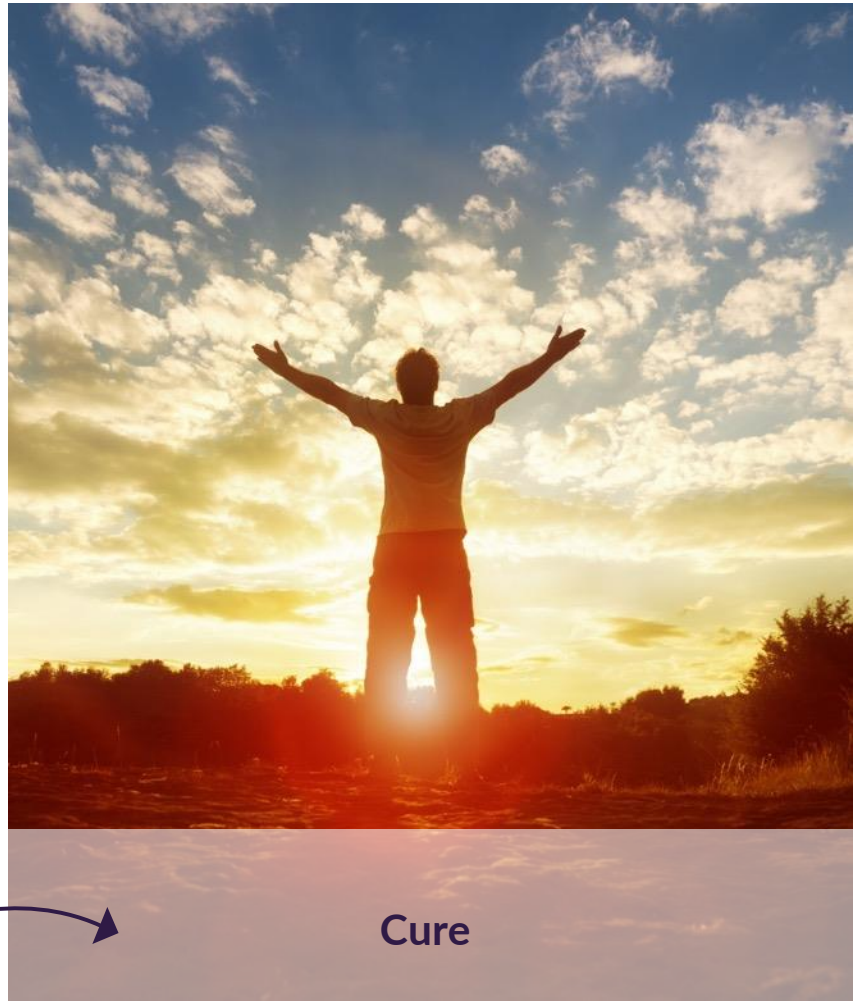
Our Treatment = Cure

Problem

Our Treatment



Cure

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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

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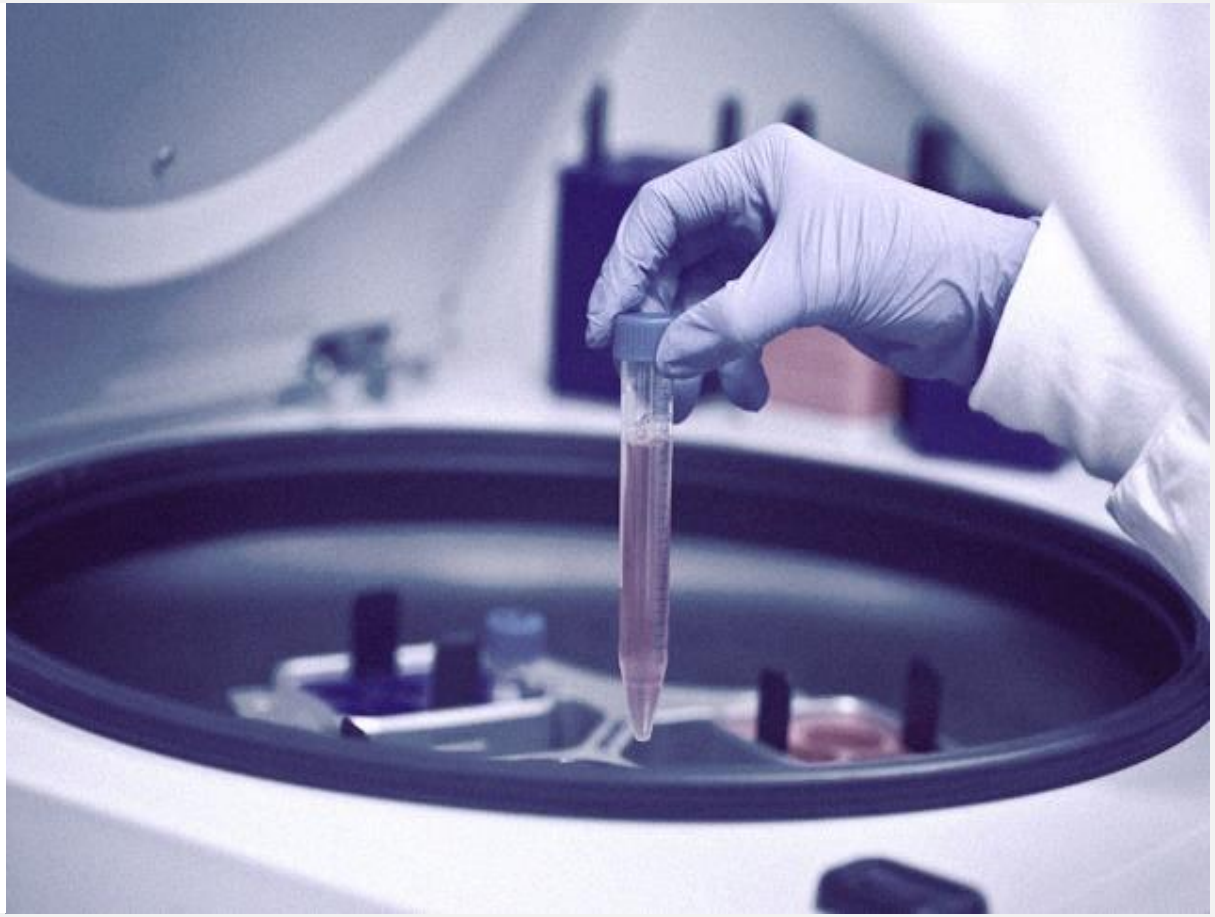
IsletRx Next Steps

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



*Initial Targeted Engagement for Regulatory Advice on CBER producTs - preliminary consultation for regulatory advice with FDA before the pre-IND consultation

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. Ariel Revel, MD

Medical Director

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.

Kfir Molakandov, PhD

VP of R&D

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Thank You.

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