



Cell Therapies that cure

May 2021 (TASE: KDST)

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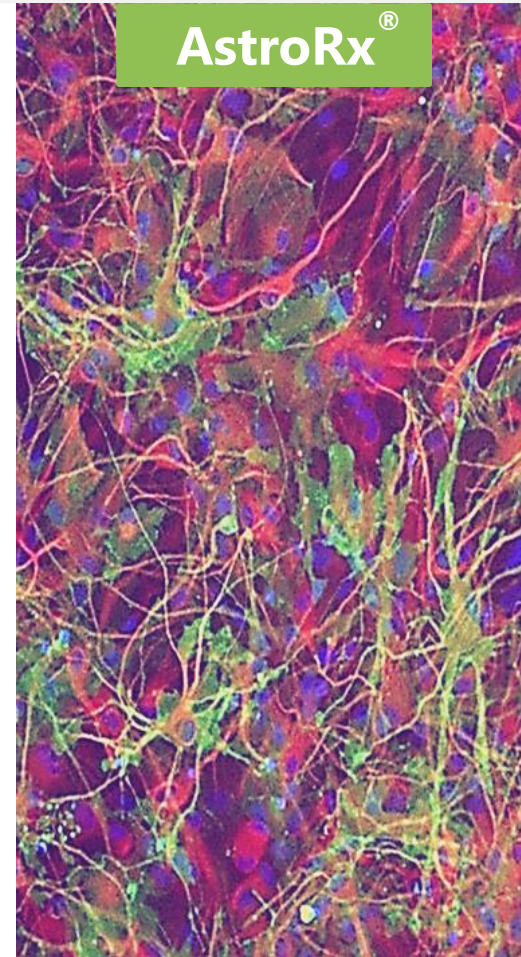
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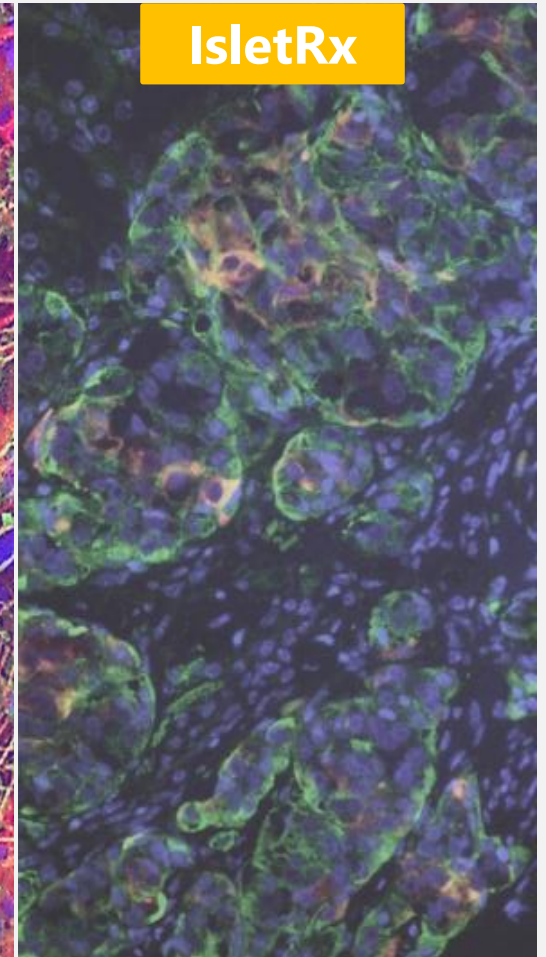
Vision – Stem Cell Derived Therapy

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

Proprietary cell lines optimized for the cure of Diabetes and to treat ALS



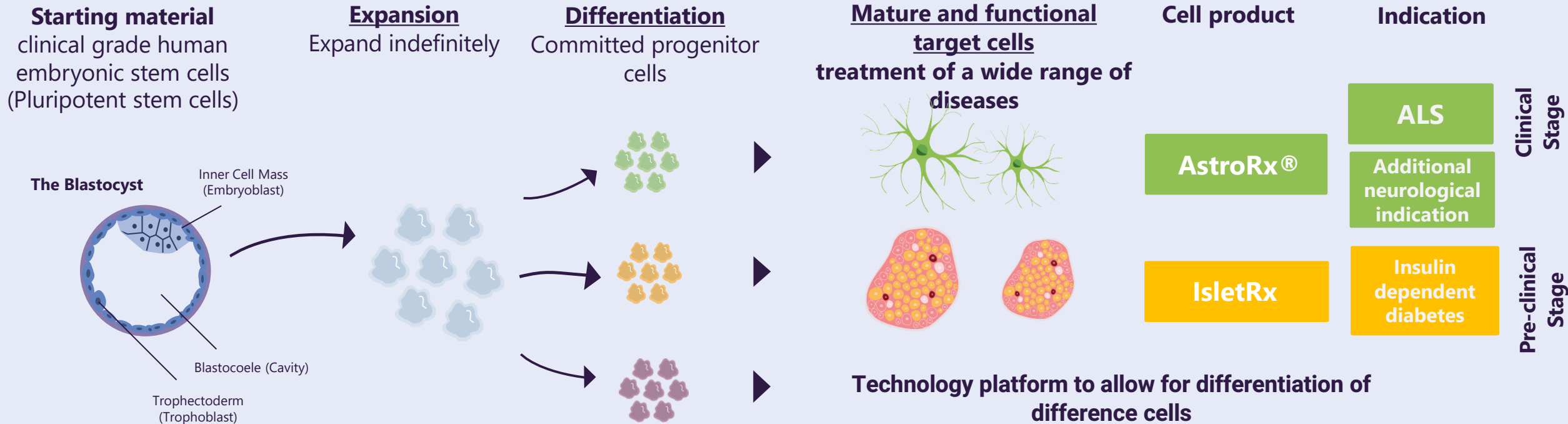
GFAP/GLAST/DAPI



C-peptide/Glucagon/DAPI

Proprietary Innovative Platform

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

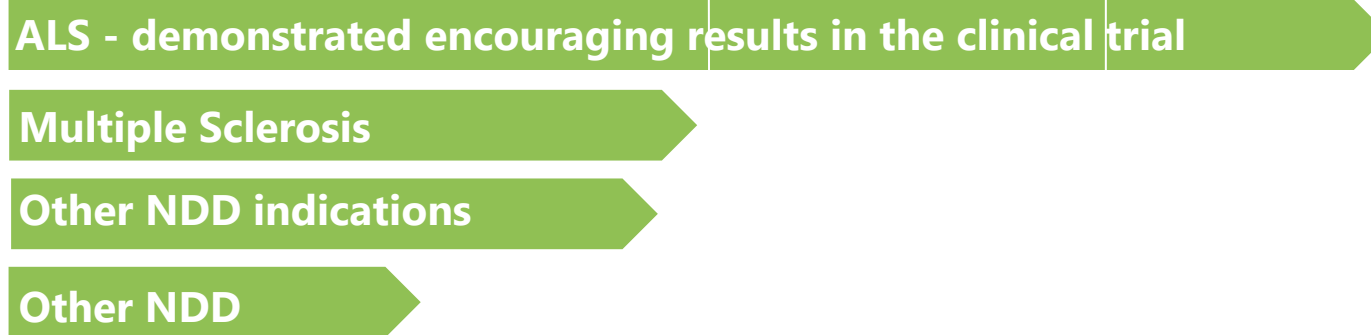


Product Platform Pipeline

CLINICAL



Neurology



- ✓ Orphan drug designation (FDA)
- ✓ Pre-IND 2015
- ✓ Completed Phase I/IIa (Isrl)

Next Pre-IND&IND for advanced clinical trial



Diabetes (Insulin dependent)



Next INTERACT (FDA)

An Active Market – Big Recent Transactions

2018

April 2018

Sigilon

Diabetes
Preclinical stage

Licensing Agreement
with Eli Lilly Co
\$473M



November 2018

Viacyte

Diabetes
Clinical stage

\$110M VC Funding
including participation of
strategic partners: JDRF,
CIRM, J&J, Gore.
\$25M Collaboration with
CRISPR.



2019

August 2019

BlueRock

Neurology
(Parkinson)
Preclinical stage

60% acquisition by Bayer
(achieving full ownership):
\$600M.



September 2019

**Semma
Therapeutics**

Diabetes
Preclinical stage

Full acquisition by
Vertex, **\$950M.**



2021

February 2021

**Sana
Biotechnology,
Inc.**

Regenerative
Cell Technology
Preclinical stage

IPO of a Regenerative
Medicine Biotech Company
at a pre-clinical stage
Proceeds of
\$587.5 M and Market
Cap. of **\$7.47 B.**



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

- <http://www.semma-tx.com/media1/vertex-to-acquire-semma-therapeutics-with-a-goal-of-developing-curative-cell-based-treatments-for-type-1-diabetes>
- <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://media.bayer.com/baynews/baynews.nsf/id/Bayer-acquires-BlueRock-Therapeutics-to-build-leading-position-in-cell-therapy>
- <https://finance.yahoo.com/news/sana-announces-up-sized-pricing-initial-042200699.html?guccounter=1>

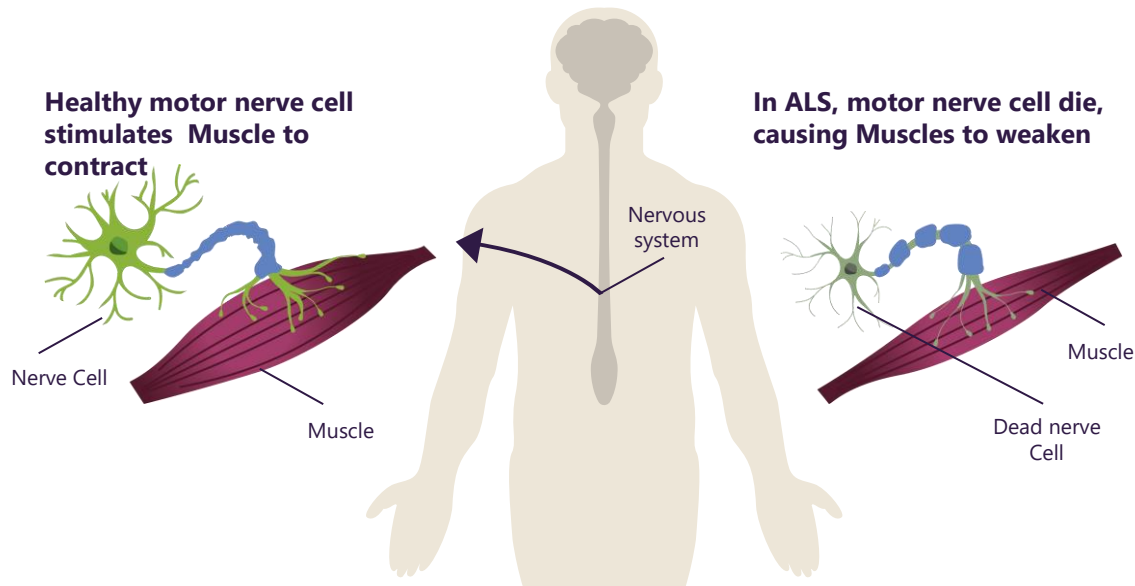
AstroRx[®]

Astrocytes 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 50-60 years, survival from onset 2-5 years



- Current FDA approved treatments are Rilutek & Radicava with modest effect

- **ALS is a fatal rare disorder with no cure**
- Around **450,000** ALS patients estimated worldwide, **30,000** patients in the US¹
- **ALS Annual drug sales:** (US, Canada, France, Germany, Italy, Spain, UK and Japan)²
 - 2019: \$282M
 - Estimate 2029: \$1.04B
- **US ALS Healthcare costs:**
 - Up to \$200K estimated annual medical expenses per patient³

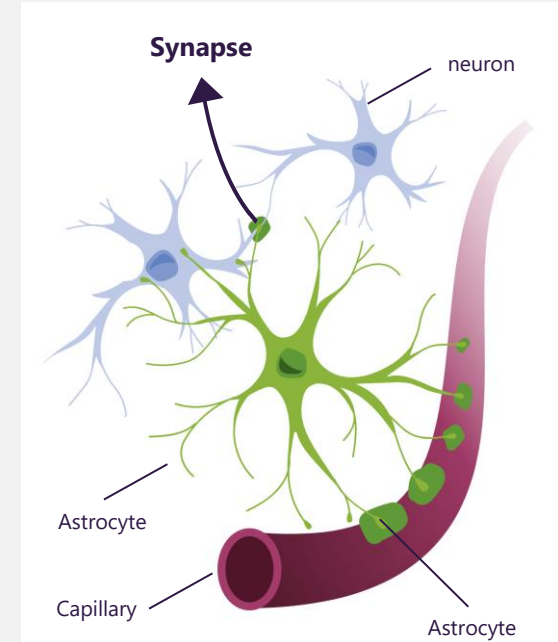


Why Use Astrocytes for ALS - AstroRx®

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	✗	✓
Remove toxic factors (i.e. glutamate)	✗	✓
Regulate oxidative stress	✗	✓
Immune-modulation	✗	✓

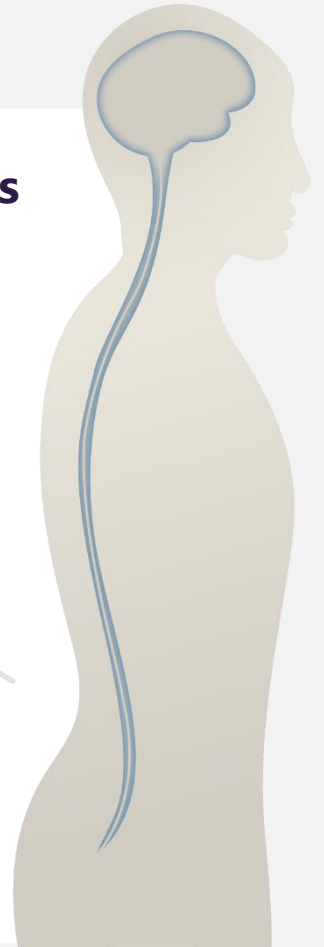
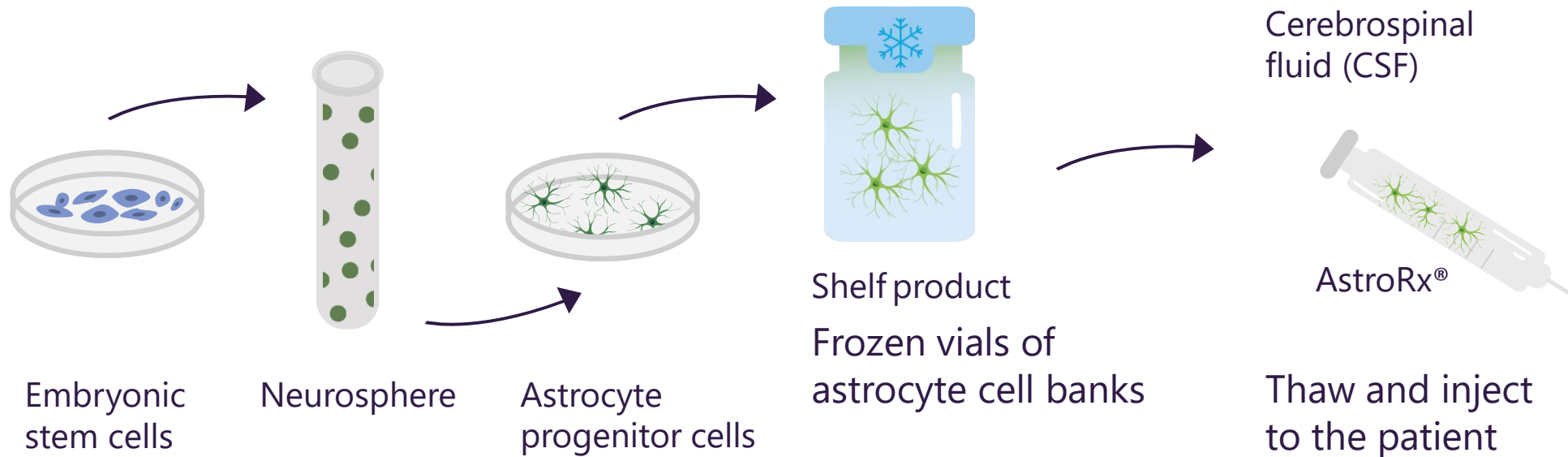


Support Motor Neurons by transplantation of healthy and functional human astrocytes - AstroRx®

Israel et al, 2020 Front. Neuroscience for review

Cell Therapy Using AstroRx® - The Process

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



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

Rat hSOD1 ALS Model:

Study measurements

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

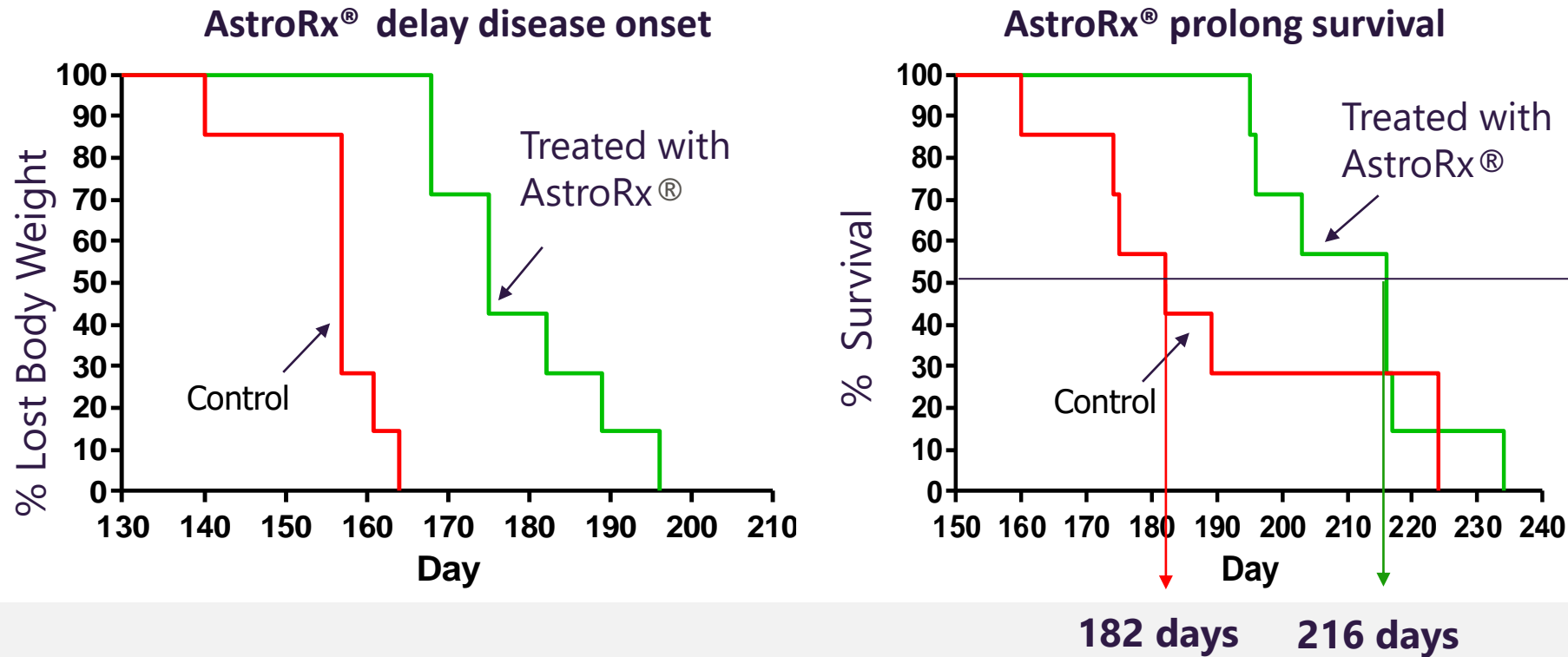
AstroRx® cells were injected at day 50 and 70 of life

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



hSOD1G93A high copy number rat (ALS model)

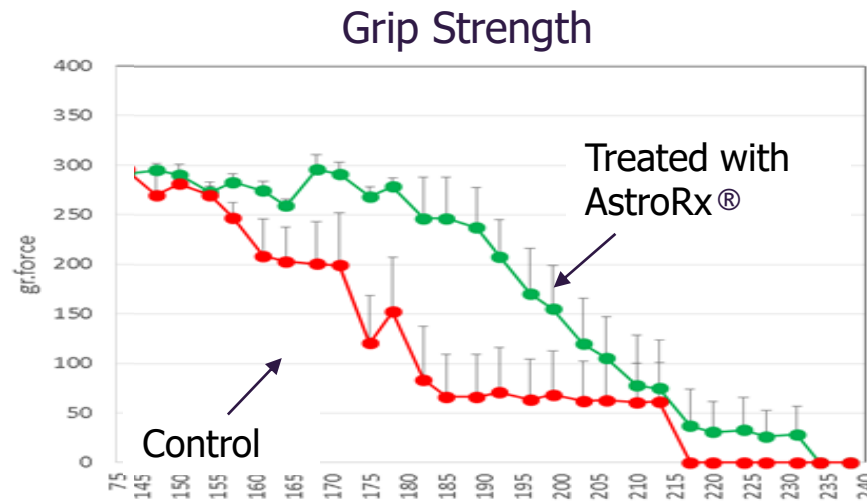
AstroRx[®] Prolong Survival of hSOD1 Rats



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

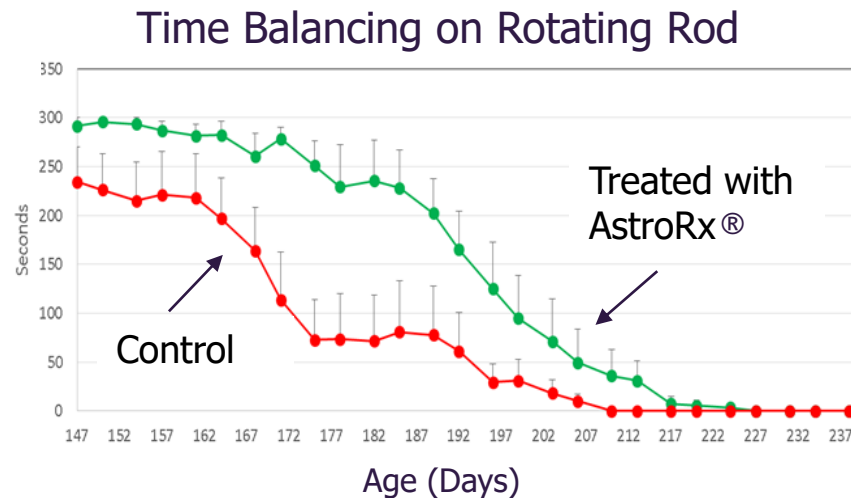
AstroRx[®] Improve Motor Performance

A



- Significant improvement in grip strength test ($P < 0.001$)

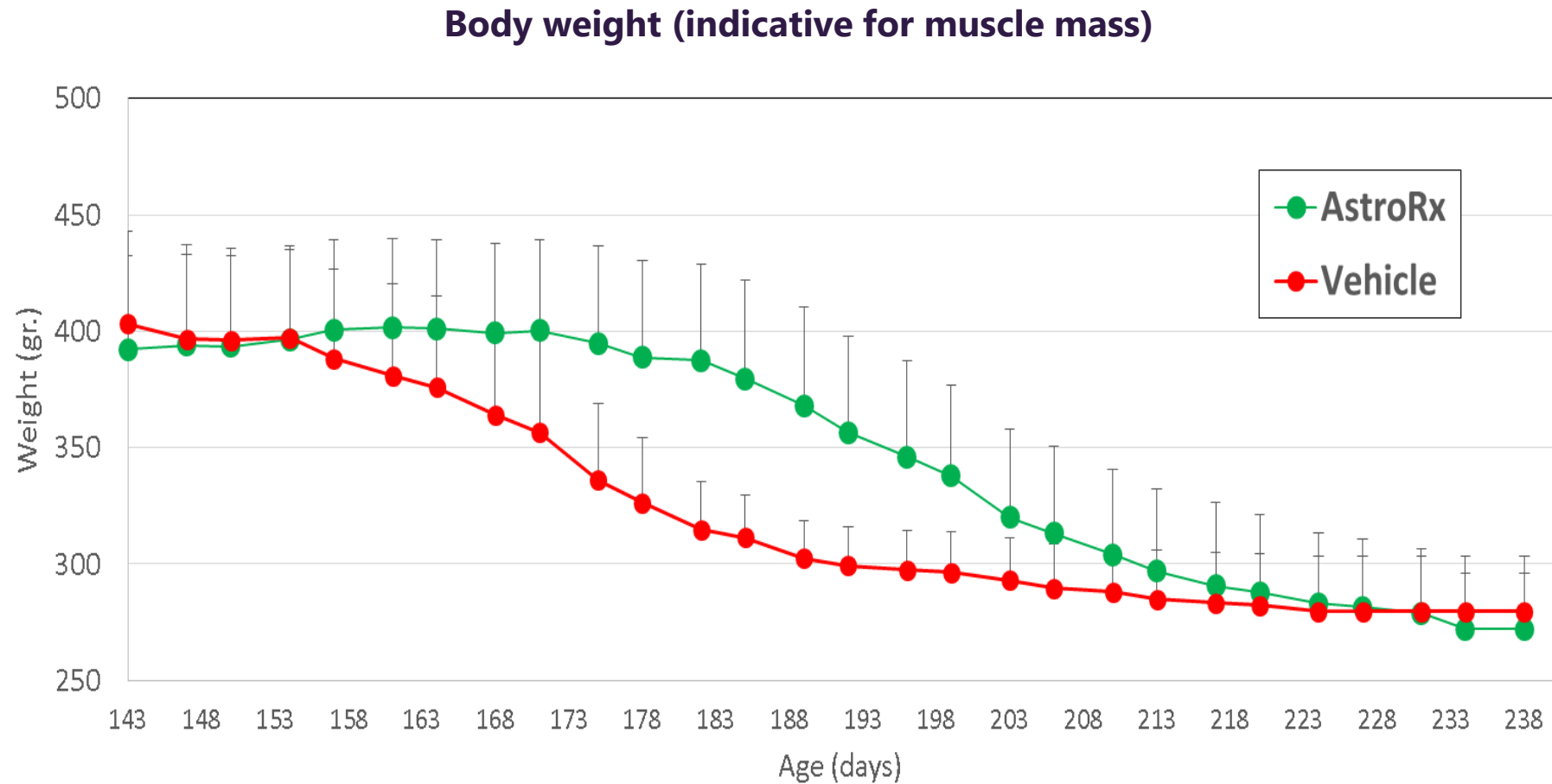
B



- Significant improvement in rotarod test ($P < 0.001$) and neurological score

Similar results were obtained in ALS mouse model

AstroRx[®] Cells Reduce Loss of Muscle Mass



Significant improvement in maintaining BW ($P < 0.05$)

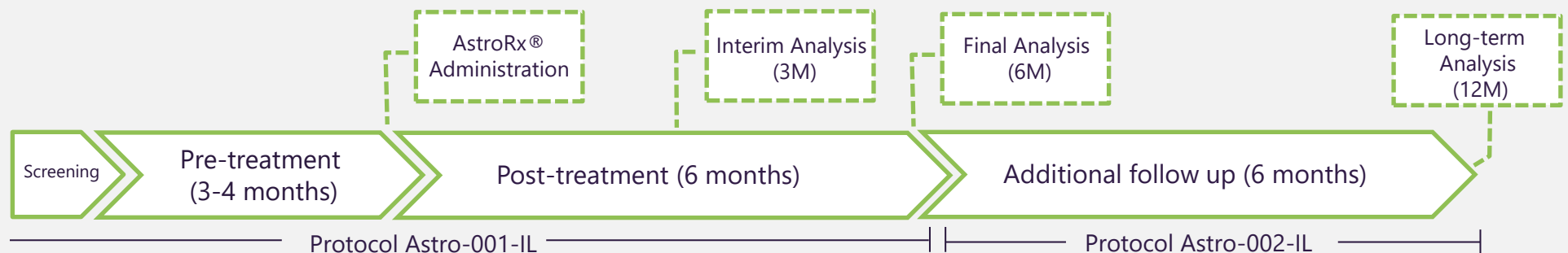
A person wearing a full-body white protective suit, a hood, and large clear safety goggles is working in a laboratory. They are wearing yellow gloves and holding a clear rectangular dish containing a red liquid. The background shows a laboratory setting with a window and a white cabinet.

In Human Clinical Trials Using AstroRx®

AstroRx[®] First-in-Human Study Design

Evaluate transplantation of astrocytes derived from Human Embryonic Stem Cells, in patients with Amyotrophic Lateral Sclerosis (ALS)

- Study Site: Hadassah Ein Kerem Hospital, Jerusalem
- Phase 1/2a, open-label, single arm per dose, dose-escalating
- A single treatment administration of AstroRx[®] was administered by intrathecal (spinal) injection to subjects with ALS at early disease stage
- AstroRx[®] doses:
 - 5 subjects in Cohort A (100×10^6 cells)
 - 5 subjects in Cohort B (250×10^6 cells)
- Study Objectives:
 - Primary: safety of escalating doses
 - Secondary: efficacy by comparing Pre- and Post-treatment assessment of disease progression



AstroRx[®] Phase 1/2a Current Status

Good Clinical Safety Profile

Study Status:

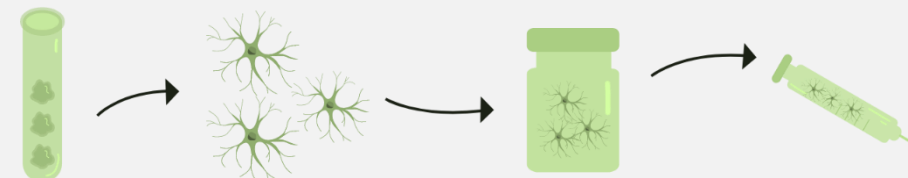
- 5 patients in Cohort A and 5 patients in Cohort B completed 6 months follow up
- Cohorts C&D were discontinued following Data Safety Monitoring Board (DSMB) recommendation due to COVID-19 pandemic

Enrollment Characteristics:

Group	Gender	Ethnicity	Mean age	ALSFRS-R at enrollment
A	5 males	Caucasian	63 ± 4.4	39.2 ± 3.5
B	4 males, 1 female	Caucasian	61 ± 5.5	40.0 ± 5.3

Safety Results:

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

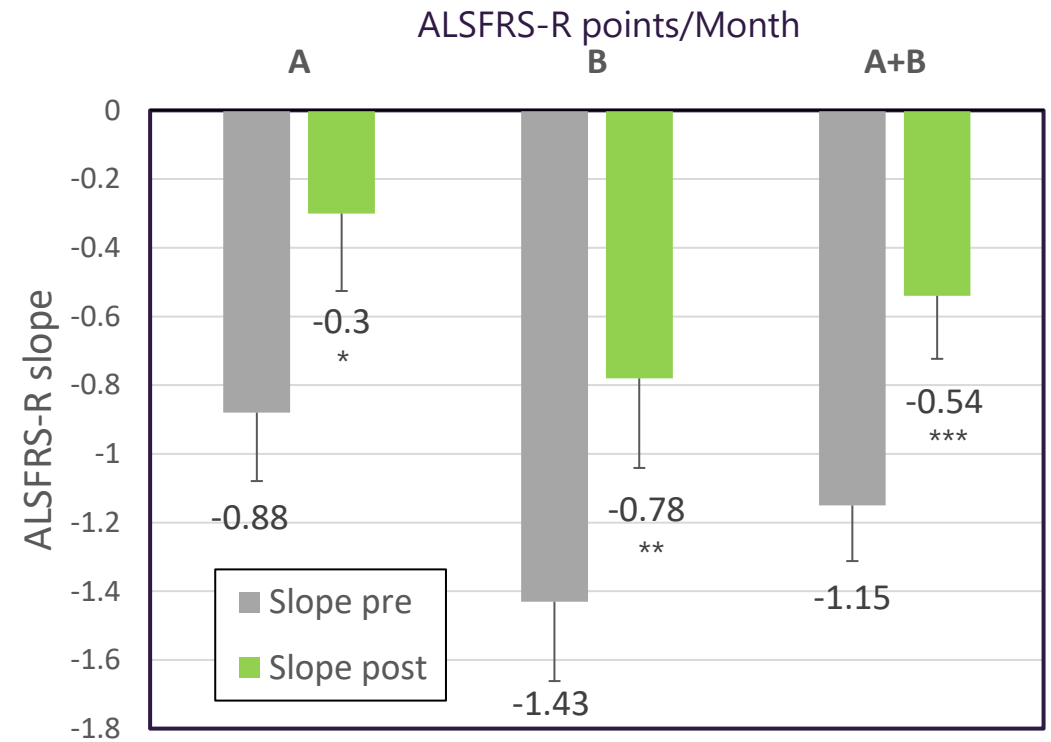


AstroRx[®] 3-month Follow-up Results

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)

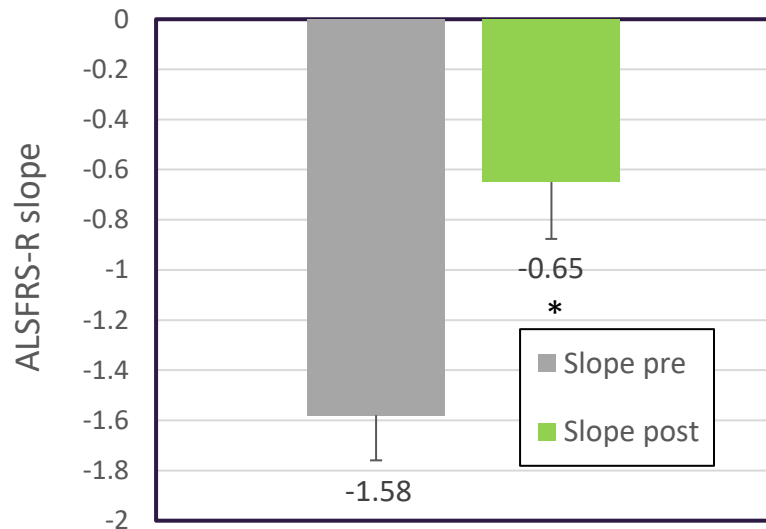
ALSFRS-R is a Clinically Accepted Measure of Disease State

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: 6-month 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 6-months
- No treatment-related serious adverse events (SAEs) nor dose-limiting toxicities were reported



AstroRx[®] Continued Safety Results

AstroRx[®] Clinical and Regulatory Plan

- A clinical development strategy to support the product intended use
- A Pre-IND meeting with FDA
- An IND supporting the approval of the next set of clinical trials
- A RMAT* designation application is planned, to enable expedited development, reviews and to accelerate approval



IsletRx

A Potential Functional Cure for Type 1 Diabetes



**IsletRx Cell
Product**

Insulin Dependent Diabetes - Market and Facts



~180 Million People
worldwide suffer from
Insulin-Dependent
Diabetes*



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



~45 million people
suffer from Type-1
Diabetes worldwide.
More than 1.1 million
are children and
adolescents (<20
years) (US >
200,000)***



High health
expenditure
Type 1 Diabetes
associated healthcare
expenditures in the US
= 16B\$ annually)**

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***

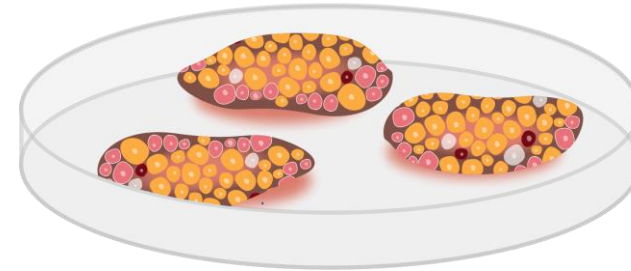


Cure for Type 1 Diabetes using IsletRx

IsletRx - Our Solution

Functional pancreatic islets from ES cells that produce and secrete insulin and glucagon

- 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**

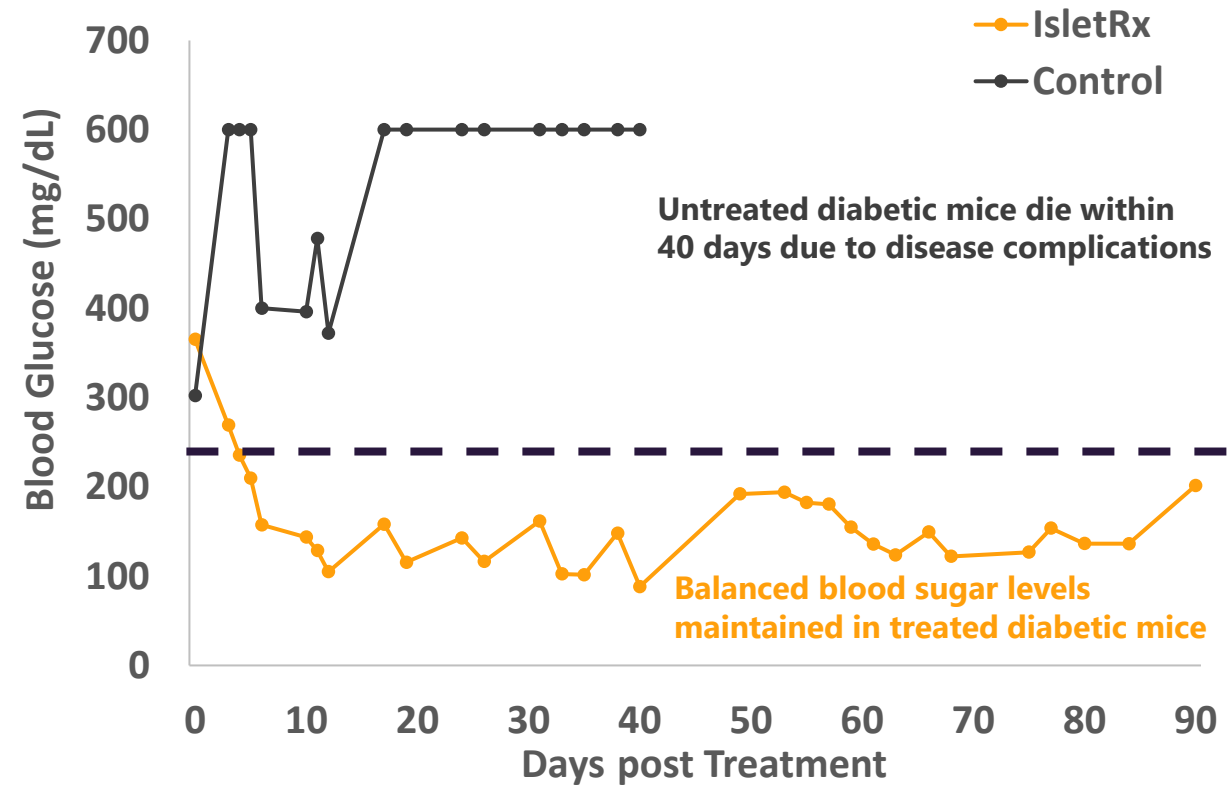


IsletRx - Preclinical Demonstration of Efficacy

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

Molakandov et al 2020, in submission



IsletRx - Production, Purification and Encapsulation

Large Scale Production:

Scalable 3D bioreactor production

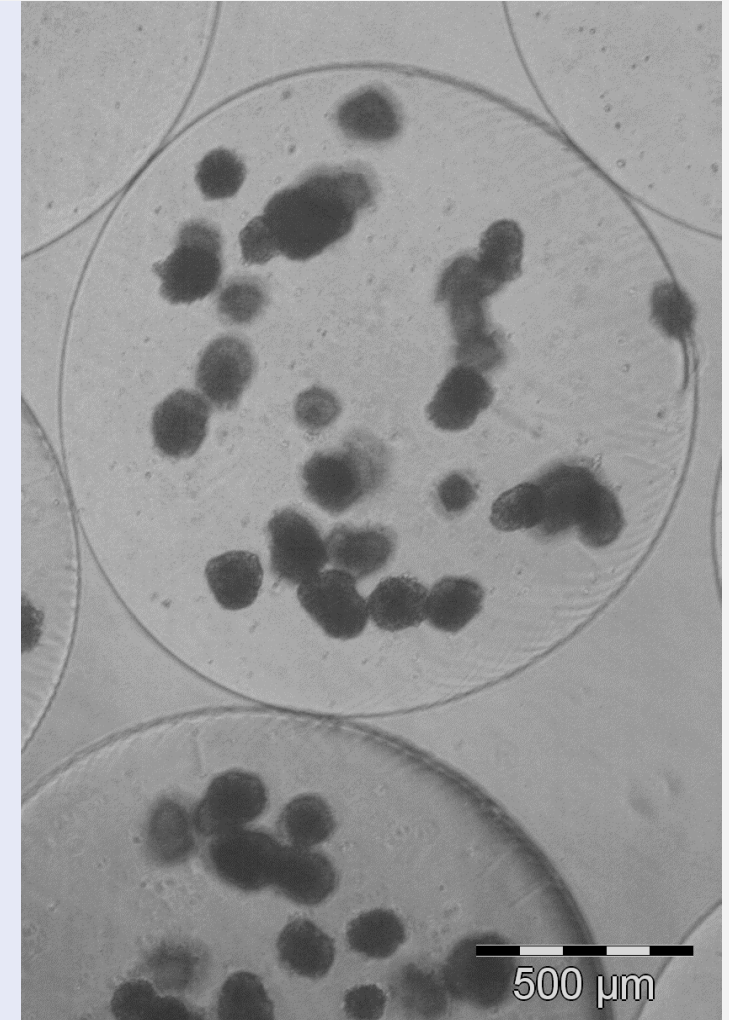
Purification & Enrichment:

Proprietary technology (IP) enables islet cell enrichment and purification, 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

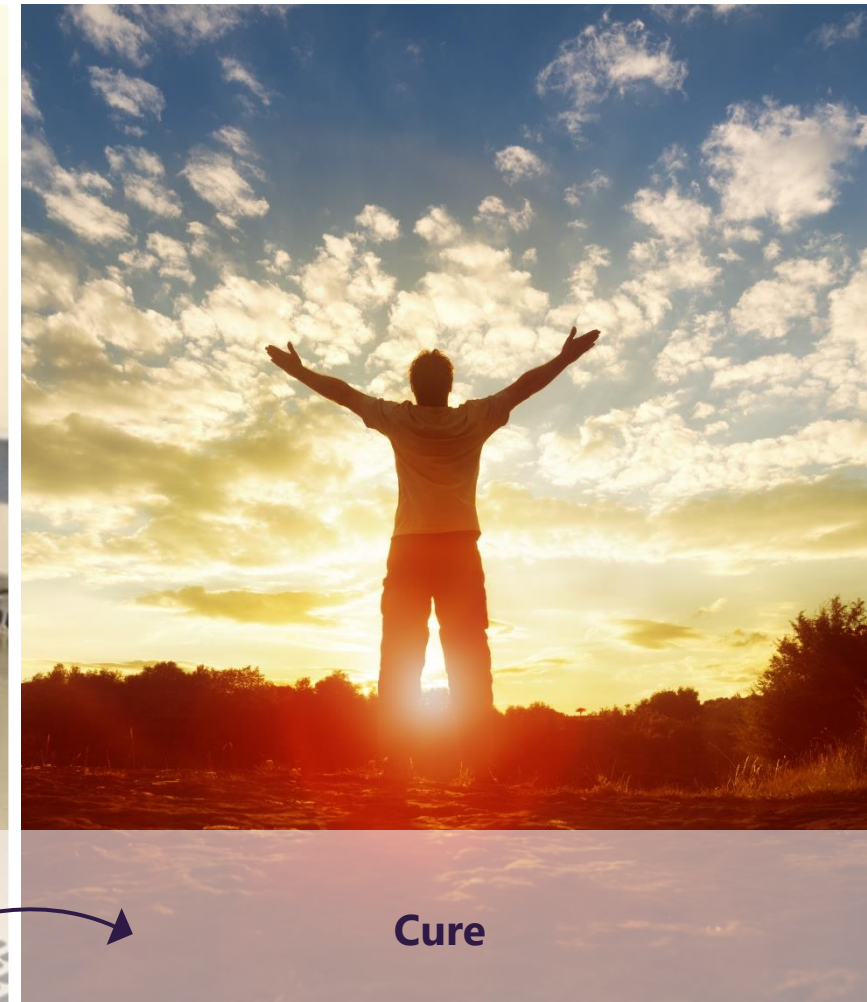
Unique Microencapsulation Technology:

*Protects **IsletRx** cells from host immune system response, overcoming a major challenge in allogeneic cell therapy*




Microencapsulated ILCs - IsletRx

Our Treatment = Cure

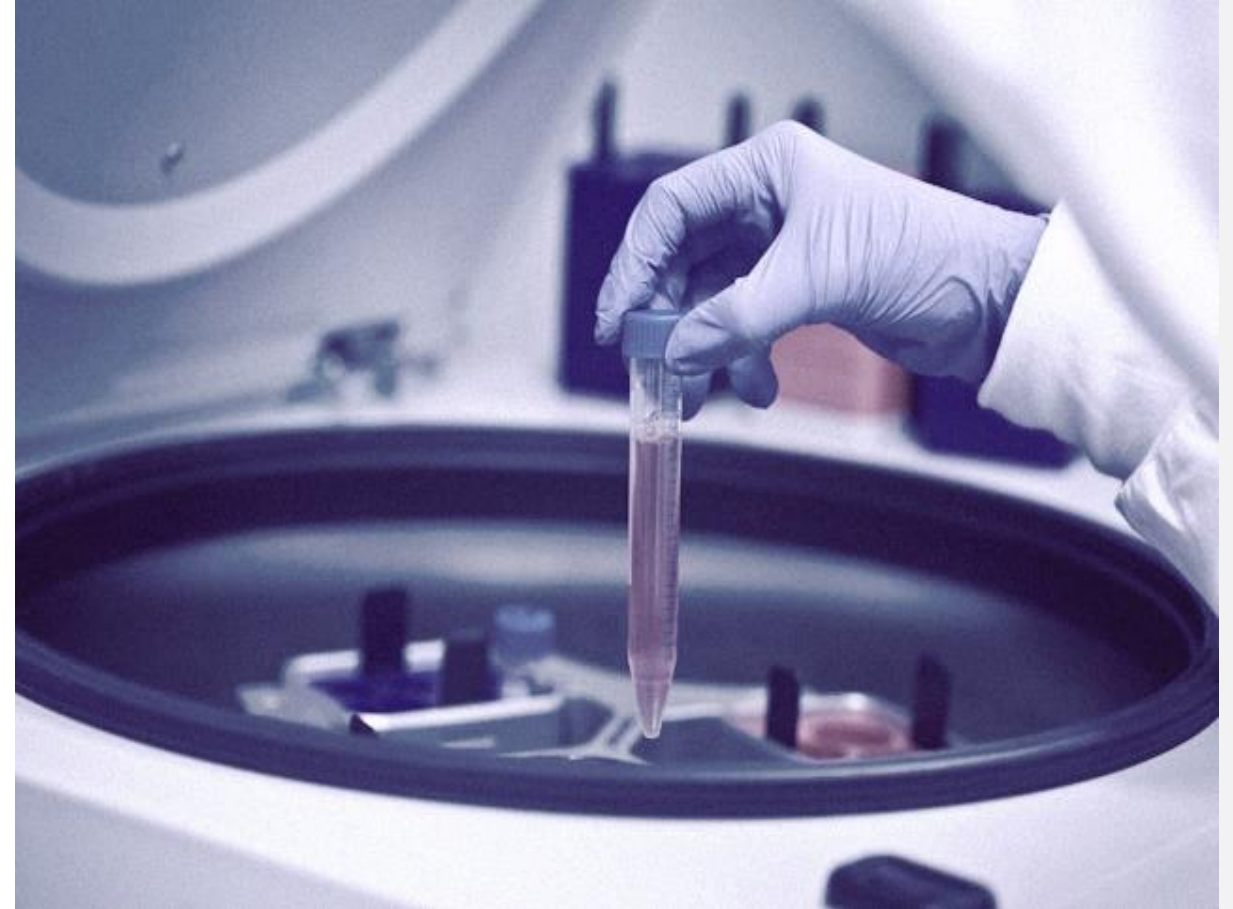


IsletRx Potential Advantages vs. Available Treatments

	 Kadimastem 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 Next Steps

- INTERACT* and Pre-IND meetings with FDA
- Implementation of 2nd generation micro and macro encapsulation products
- Upscaling and GMP production



Leadership

Bringing extensive business, industry, and scientific experience



Prof. Michel Revel
Founder & CSO

- Developed Merck's blockbuster drug REBIF® for multiple sclerosis (\$1.7B USD in sales in 2016)
- Professor Emeritus of molecular genetics at the Weizmann Institute of Science
- More than 40 years of experience in development and global commercialization of advanced biotechnological products
- Awarded Laureate of Israel Prize for Medicine in 1999 and EMET Prize for Science in 2004



Asaf Shiloni
CEO

- More than 20 years of biotech executive experience and a deep knowledge of the cell therapy industry
- Mr. Shiloni served as Vice President Sales and Business development at PeproTech for 13 years, there he established collaborations and joint ventures with top US stem cell companies and leading research labs worldwide as well as led M&A processes
- Prior to PeproTech, in 2007, Mr. Shiloni sold an Israeli biotech company CytoLab, that he co-founded and led for seven years
- Mr. Shiloni holds a BA in Computer Information Systems and Business from The College of Management and an MBA from Tel Aviv University

Leadership



Asaf Shiloni
CEO



Yossi Nizhar
CFO



Arik Hasson, PhD
VP of Business Development



Prof. Michel Revel
Founder & CSO



Michal Izrael, PhD
VP R&D



Kfir Molakandov, PhD
Director of Diabetes Research and Innovation



Ronen Twito CPA
Chairman of the Board



Veronique Bellaiche
Director of Regulatory Affairs and
Quality Assurance

Thank You.



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