Celavie™ Biosciences

Novel Stem Cell Therapy for Restorative Treatment of Degenerative Disorders

Sandy Solmon, CEO

Mission

Deliver effective new restorative treatments for **Parkinson's disease, Cerebellar Ataxia**, and others that have no curative therapies.

Agenda

1. Overview of our proprietary technology
2. GMP closed manufacturing System
3. Parkinson's Disease Indication
4. Cerebellar Ataxia Orphan Indication
5. Product Development Strategy and Timeline

Celavie Stem Cells are Unique

01 Allogeneic pluripotent cells used in an undifferentiated and unmodified state

02 In an undifferentiated state, Celavet cells are able to read the microenvironment and differentiate into various mature cells corresponding to specific anatomical structure

03 Our cells are non-tumorigenic and hypo-immunogenic

04 Override malign signals from genes

05 Secrete paracrine factors

06 Stimulate hosts own protective and regenerative pathways

07 Restore function in multifactorial neurodegenerative disease

Safety Evidence in Clinical and Pre-Clinical Studies

Celavie's stem cells are:

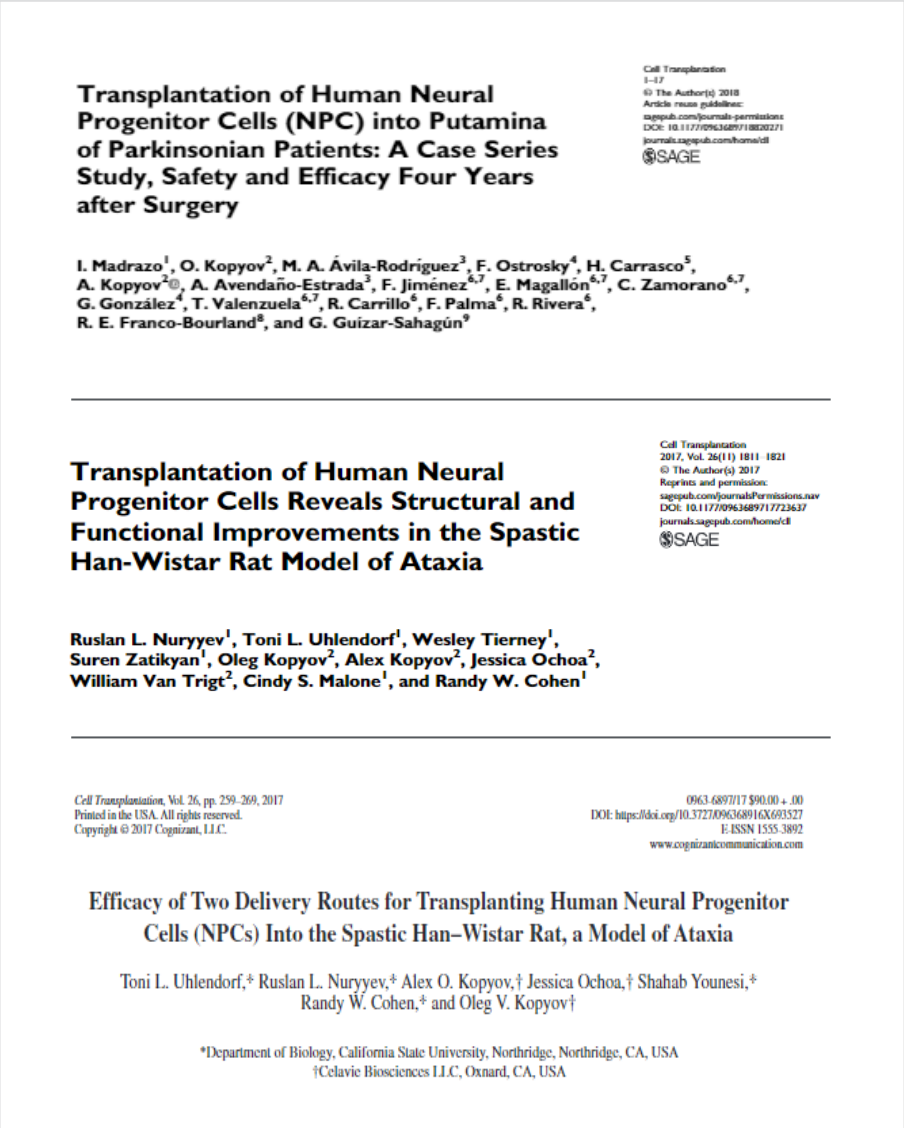
- ✔ Pure/homogeneous
- ✔ Genetically stable over multiple passages
- ✔ Independent of dosing

"First-in-Human" trial having 5-year follow-up demonstrates Celavie stem cells produced:

No Tumor Formation

No Immune Response

No Dyskinesia in PD



Transplantation of Human Neural Progenitor Cells (NPC) into Putamina of Parkinsonian Patients: A Case Series Study, Safety and Efficacy Four Years after Surgery

Cell Transplantation
1–17
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Transplantation of Human Neural Progenitor Cells Reveals Structural and Functional Improvements in the Spastic Han-Wistar Rat Model of Ataxia

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Efficacy of Two Delivery Routes for Transplanting Human Neural Progenitor Cells (NPCs) Into the Spastic Han–Wistar Rat, a Model of Ataxia

Toni L. Uhlendorf,* Ruslan L. Nuryyev,* Alex O. Kopyov,† Jessica Ochoa,† Shahab Younesi,* Randy W. Cohen,* and Oleg V. Kopyov†

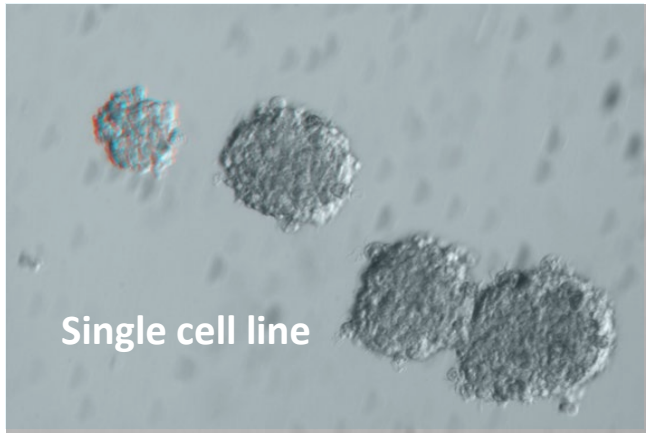
*Department of Biology, California State University, Northridge, Northridge, CA, USA
†Celavie Biosciences LLC, Oxnard, CA, USA

cGMP Platform Manufacturing System

Commercial Scale cGMP Production of Clinical Grade Stem Cells

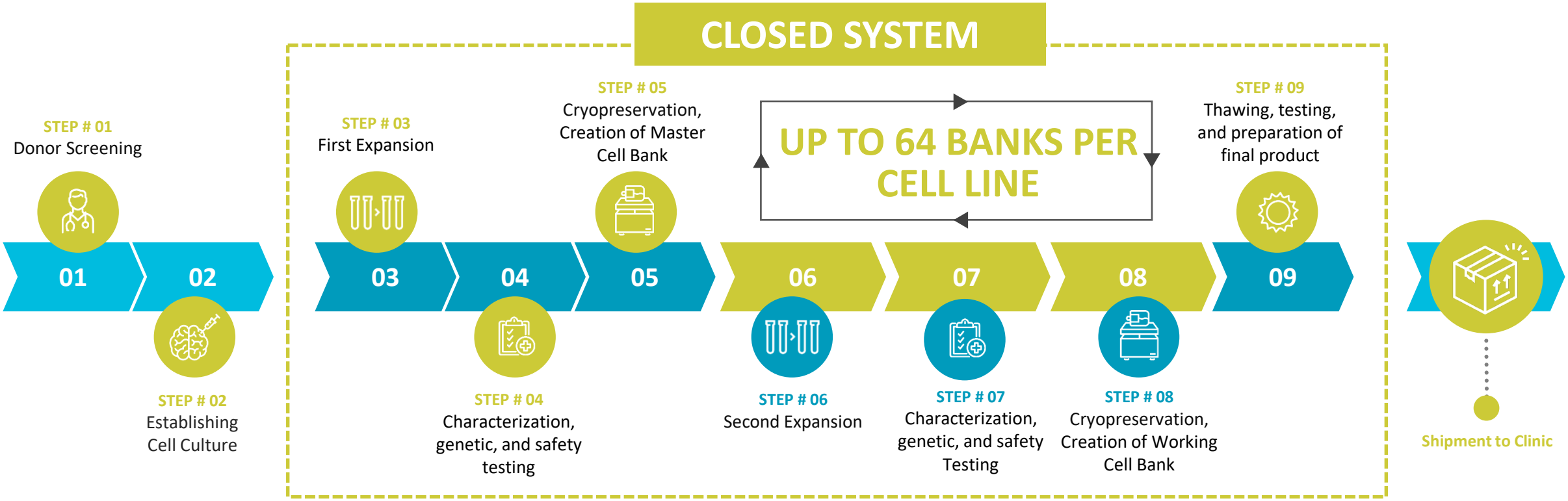
- cGMP manufacturing center in California
- Industry-accepted, multi-tier cell banking system
- Meets stringent FDA/CVM guidelines for viability, genetic stability and absence of infectious agents
- All species cell banks are produced utilizing the same methodology

- Proprietary isolation technology designed in collaboration with Comecer America
  - cGMP compliant
- Commercial-scale production and banking of cells
- Produces highly standardized, genetically stable cell lines, with uniform phenotypic characteristics



1M
Therapeutic Doses

Celavie Platform Manufacturing Process



Celavie has created a PLATFORM cell banking and manufacturing process.
Same cell bank for all indications. Only site and mode of injection will change.

Spastic Rat Model of Cerebellar Ataxia has Similarities with Idiopathic Parkinson's Disease

- ✔ Next Generation DNA sequencing revealed multigenetic profile
- ✔ Spontaneous development;
- ✔ Clinical symptomatology: forelimb tremor, hind-leg rigidity, gait abnormality

Ataxia Mutations

Relevance	Gene
SCA5	B III Spectrin (SPTBN2)
SCA1	ATXN1
Friedreich's Ataxia	FXN
Developmental Ataxia	SOX4
SCA19/22	KCND3

PD Mutations

Relevance	Gene
Idiopathic PD	GBA
SCA1	HTRA2
Synuclein	PARK2
Synuclein	PLD1

All mutations are high or medium impact variant mutations

Mechanisms of Action: Paracrine Effect of OK99 Results in Increase in Number of Host's Purkinje Cells

OK99 acts by secreting biologically active substances which promote healing:

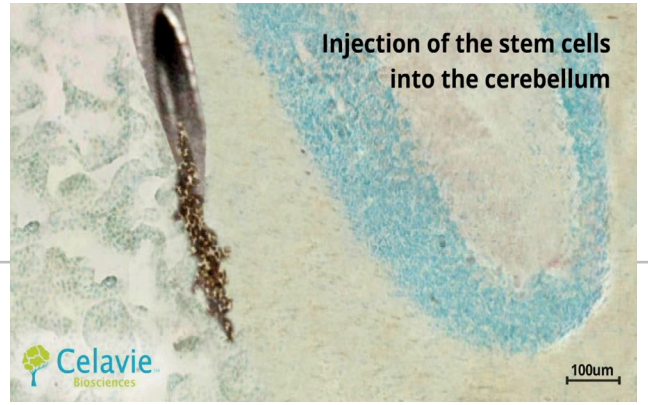
- ✓ **Neuromodulin** - promotes neuronal growth, plasticity protection
- ✓ **14-3-3 Epsilon Protein** – reduces neurotoxicity induced cell death.
- ✓ **Insulin Like Growth Factor II** - Neuroprotective effect in aging brain
- ✓ **Activity Dependent Neuroprotective Protein** - Down-regulation contribute to dopaminergic neurodegeneration in PD
- ✓ **Ceruloplasmin** - Injections were shown to reverse cell death in substantia nigra (PD).

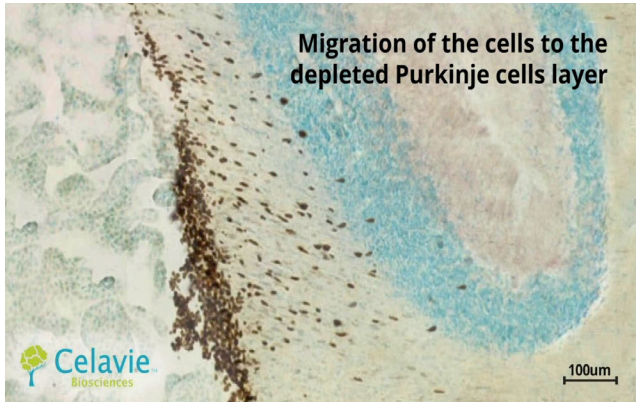
Proteomics study by National Research Council of Canada

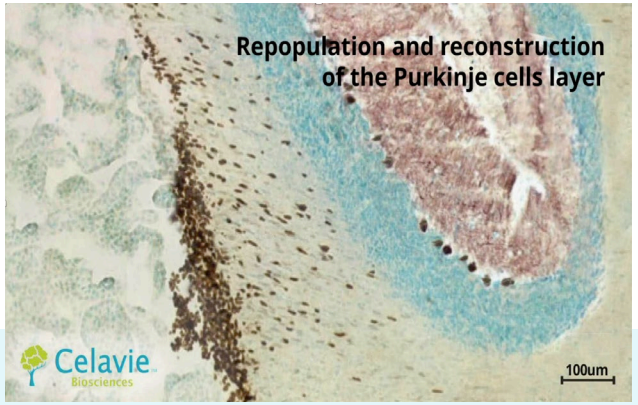
Results confirmed + quantified with Elisa

Celavie Cells Migrate to Site of Degeneration and Differentiate into Functional Neurons

- ✔ Spastic Hans Wistar rats are model of Cerebellar Ataxia
- ✔ Treated rats became asymptomatic in all four pre-clinical studies
- ✔ 3 manuscripts in peer-reviewed journal***, Cell Transplantation***
- ✔ Demonstrates **differentiation** according to nature of damage
- ✔ Demonstrates cells **override malign signals** from mutated genes





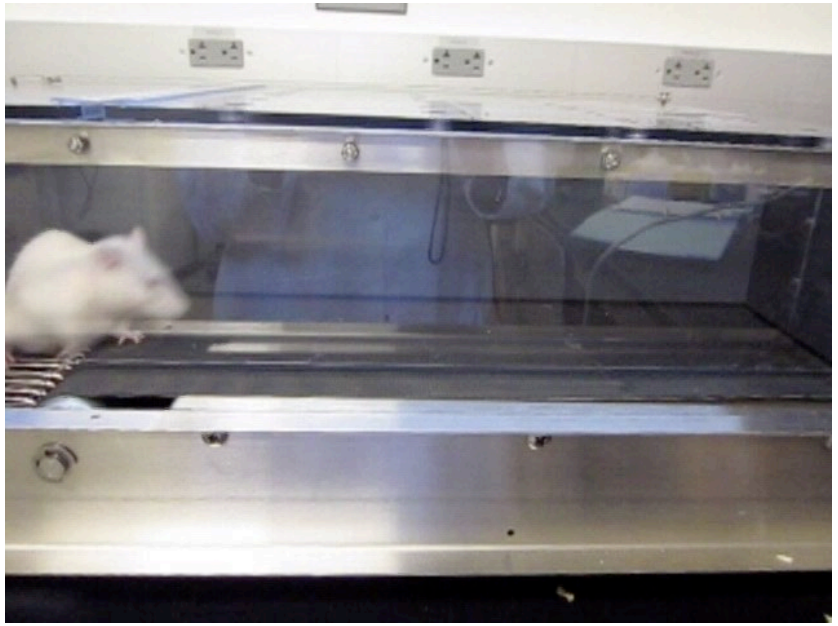


This example is made from sequential brain slices of a euthanized rat 30 days post treatment

Clinical Effects of Transplantation of Celavie Stem Cells

▲ PLAY

Non-treated control animal cannot perform on the treadmill test.



▲ PLAY

30 days after the Celavie OK99 stem cell injection, an experimental mutant animal ***can perform the treadmill test.***

Published in *Cell Transplantation* Journal, Feb. and June 2017:

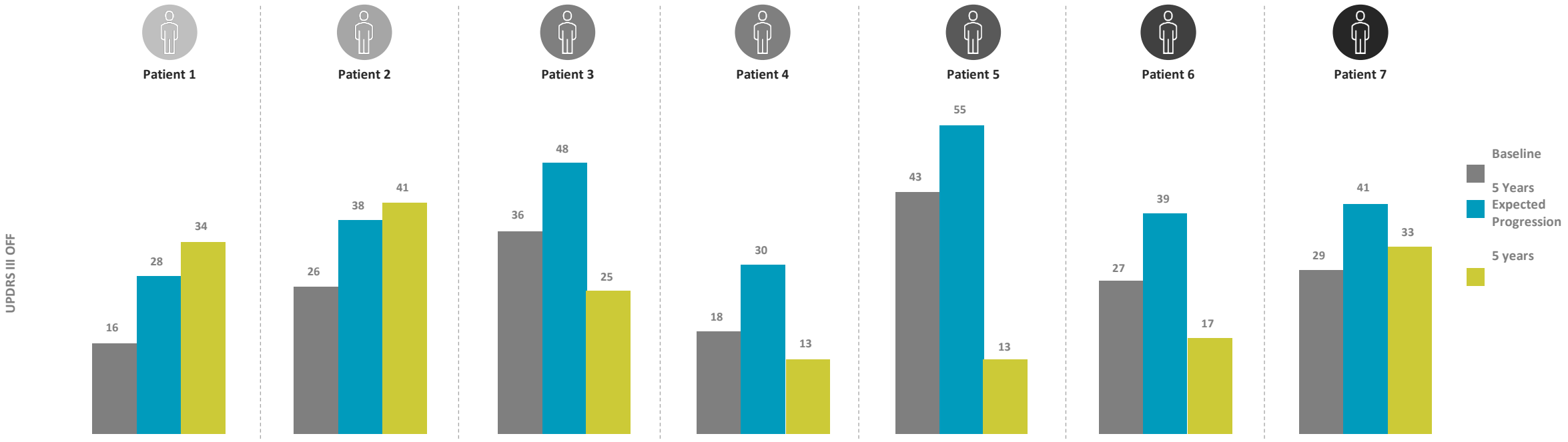
"Transplantation of Human Neural Progenitor Cells Reveals Structural and Functional Improvements in the Spastic Han-Wistar Rat Model of Ataxia"

"Efficacy of Two Delivery Routes for Transplanting Human Neural Progenitor Cells (NPC's) Into the Spastic Han-Wistar Rat, a Model of Ataxia"

Parkinson’s Disease Treatment

5 of 7 Parkinson's Disease Patients Showed Improvement Over Expected Progression After 5 Years Off Medication

Measured by UPDRS III – Parkinson's Disease Rating Scale

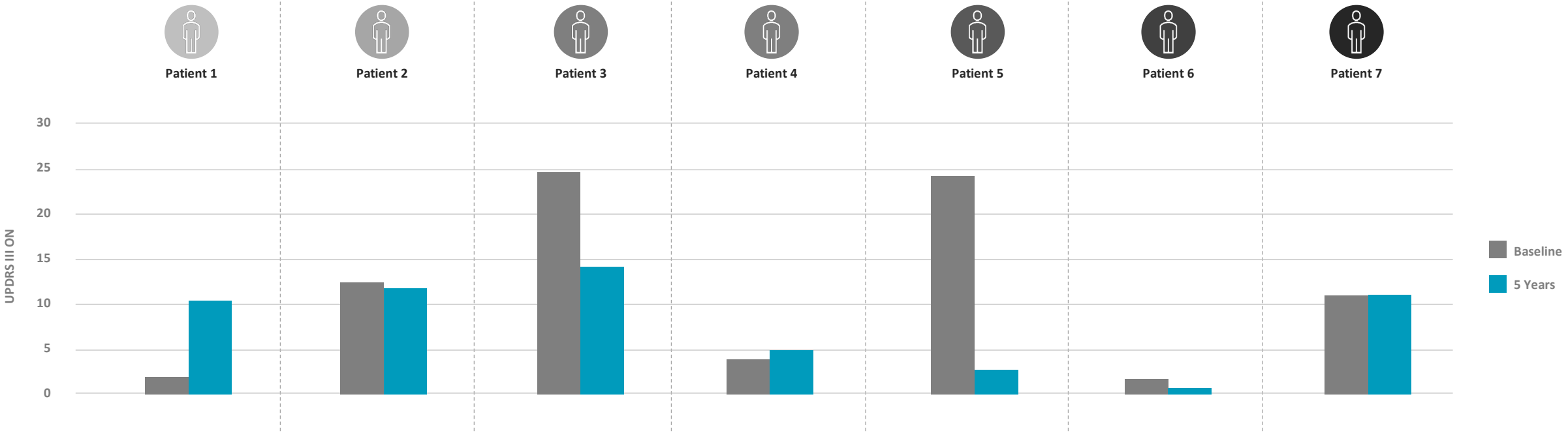


Average UPDRS III Progression - 2.4 Points/Year

*2.4 mean OFF yearly deterioration. Holden SK, Finseth T, Sillau SH, Berman BD. Progression of MDS-UPDRS Scores Over Five Years in De Novo Parkinson Disease from the Parkinson's Progression Markers Initiative Cohort. Mov. Disord. Clin. Pract. 2017;5(1):47–53.

5 of 7 Parkinson's Disease Patients also had *Improved Response* to Medication

Measured by UPDRS III – Parkinson's Disease Rating Scale



Medication Changes	1000mg to 1750mg	1000mg to 1870mg	1300mg to 1000mg	1250mg to 1200mg	1687mg to 1110mg	625mg to 625mg	1550mg to 1250mg

Patient with dyskinesia 5yrs responsive to medication

Cerebellar Ataxia Indication

Spinocerebellar Ataxia Development Program

- ✔ **File for Orphan Drug Designation**
- ✔ **Phase 1 Open Label Study**

Conduct: Hoag Memorial Hospital Presbyterian, Newport Beach, CA;

Time frame: Two years

Methodology: Pilot open-label, randomized safety study for the treatment of SCA1.
8 patients in experimental group; 8 patients in the matched control.

Primary end-point is safety: Secondary measures include variable neurological, neuropsychological and radiological evaluations.

Status: Principle Investigator: Dr. Susan Perlman, UCLA David Geffen School of Medicine
Medical Director of the National Ataxia Foundation.

Celavet

Applications in Veterinary Medicine

Celavet Focus

Celavet Initial Focus Targets Different Diseases and Injuries for Each Species

Equine – tendon and ligament injuries

Canine – Osteoarthritis, Epilepsy and Cruciate Ligament injuries

Feline – Renal Disease

Biosimilarity Of Different Species' Mammalian Cells Produced With Celavie / Celavet Technology

01 Celavie technology allows production of cell lines from multiple mammalian species that are phenotypically and functionally similar, with the similar standard values of purity, potency and genetic stability

02 Similar expression of stem cell markers

03 Similar secretion of biologically active factors as confirmed by proteomics analysis

04 Similar phenotype translates into similar functional capabilities independent of species of origin

05 Celavie stem cells are unmodified, undifferentiated and dose independent.

06 Undifferentiated stem cells allow for the treatment of multiple, diverse pathologic conditions across a range of species

07 Multiple pre-clinical and clinical experiments demonstrate that Celavie/Celavet stem cells have successfully treated musculoskeletal and neural system disorders in various animal species

Celavet Development Milestones

- ✓ Randomized, double-blind, controlled study, Cornell (8 horses)
- ✓ Published Manuscript (Stem Cell Research & Therapy: *Fetal derived embryonic-like stem cells improve healing in a large animal flexor tendonitis model*)
- ✓ INAD "OK100 for the Treatment of Equine Musculoskeletal Injuries" - 400 Case Open Label Study*
- ✓ INAD for Osteoarthritis, Epilepsy, Cruciate Ligaments

- ✓ Donor Screening Protocol Approved*
- ✓ Product Characterization Approved*
- ✓ Potency Assay Developed
- ✓ Large Scale Stem Cell Production Methodology Developed
- ✓ Open Label Pilot in 35 dogs for Osteoarthritis, Epilepsy, Cruciate Ligaments showed safety and encouraging results
- ✓ Compassionate use (CVM/FDA) for canine burn victim

- ☐ Pivotal Study Protocol - INAD "OK100 for the Treatment of Equine Musculoskeletal Injuries"
- ☐ Target Animal Safety Study Protocol
- ☐ Pivotal Study Approval - INAD "OK100 for the Treatment of Equine Musculoskeletal Injuries"
- ☐ Target Animal Safety Study Approval
- ☐ Apply for ECAP/MUMS for one or more development programs

2009 - 2018 → **2020**

Celavie Summary

Corporate Objectives and Capital Requirements

Celavie Stem Cells Are Unique

Celavie

Parkinsons

Treatment:

- ✓ **Dopamine deficiency:** Motor impairment
- ✓ **Serotonin deficiency:** Motor and non-motor impairment *(the latter - cognitive decline, mood changes)*
- ✓ **Acethylcholine surplus**: Dementia
- ✓ **Glutamate surplus:** Exitotoxicity *(further neronal degeneration)*

Competitor

Parkinsons

Treatment:

- ✓ **Dopamine deficiency:** Motor impairment
- X **Serotonin deficiency:** Motor and non-motor impairment *(the latter - cognitive decline, mood changes)*
- X **Acethylcholine surplus**: Dementia
- X **Glutamate surplus:** Exitotoxicity *(further neronal degeneration)*

Holistic approach: Ability of the undifferentiated cell to address a complex disease, like PD, in entirety. Celavie cells are low cost per dose to manufacture.

Pre-differentiated cells can address only one component of the disease and require impossible knowledge of how many cells are necessary for an individual patient. Gene therapies and Mesenchymal cells are costly per dose to manufacture.

Achievements, and Objectives Through 2021

2019

- ✓ Peer Review Publication: PD trial 4-year results (Human)
- ✓ Publication Submitted: Long term efficacy of OK99 in rat model of CA
- ✓ Upgrade GMP facility
- ✓ New GMP grade production line
- ✓ Pre-IND meeting, Phase I Parkinson's Disease

2020

- ☐ Follow up data on Parkinson's study (5-year)
- ☐ FDA pre-IND conference for Phase I Ataxia
- ☐ Additional safety and proof-of-concept studies
- ☐ File US IND for Parkinson's Disease
- ☐ Initiate Phase I Parkinson's Disease Trial in US

2021

- ☐ Apply for orphan drug, Cerebellar Ataxia in collaboration with National Ataxia Centre
- ☐ Initiate Phase I Cerebellar Ataxia Trial in US
- ☐ Equine Tendonitis Trial in US (Celavet)

Capital Requirements and Use of Funds

Seed money from serial entrepreneur and efficient use of capital to date

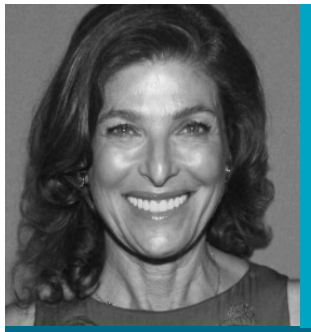
Seeking non-dilutive grant monies and strategic partnerships to fund clinical development

Clinical and regulatory plan to take advantage of government and regulatory incentives

Dual track approach in Parkinson's and Ataxia provides faster track to commercialization

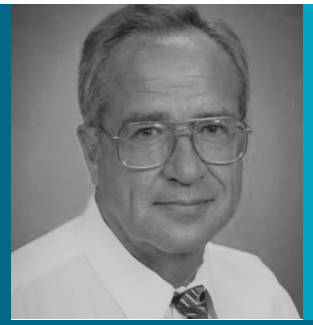
Actively seeking to out license Celavet veterinary application and/or partnerships on human therapeutic development

Team



Sandy Solmon
CEO and President

Christopher Duma, MD, FACS
Principal Investigator, Phase I Trial and Clinical Advisor

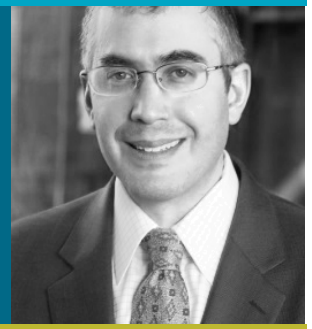


Oleg Kopyov, MD, PhD
Executive Vice President and Chief Scientific Officer

James Robinson
Sr. Consultant Manufacturing and Regulatory Advisor

Alex Kopyov
Vice President of Clinical R&D

DLA Piper USA LLP
Howard Schwartz
Legal Advisor



CLEMENTI ASSOCIATES

LaVoieHealthScience
Strategic Communications

Clementi Associates, Ltd
Medical and Regulatory Advisor

LaVoie Health Science
Public and Investor Relations

A team of dedicated experts with passion to disrupt healthcare.

Celavie™ Biosciences

Thank You

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Celavie™
Biosciences

Appendix

UPDATED 9/6/2019

Market Opportunity for PD

1 mil

PD Patients US

300

US Surgical Centers doing DBS

50,000

Stem Cell Procedures/yr

$2.5 Bil

US Potential

Per Metronix, cost of DBS device is $25K

Note: Conservative estimates for penetration and pricing ($50K)

Phase I US Clinical Trial Planning Underway

Double-blind Placebo Controlled Randomized Trial in US

Purpose: To evaluate the safety of Celavie's stem cells in treating patients suffering from Parkinson's disease

Conduct: Hoag Memorial Hospital Presbyterian, Newport Beach, CA

Time frame: 3 years

Methodology: This will be a two-part study, wherein Part I is a staggered-start open label longitude trial, and Part II is a randomized, two arm, double-blind, controlled, longitudinal trial of Celavie stem cells for the treatment of moderate to advanced Parkinson's Disease. Stage II will be launched only if 3 month follow up of the patients enrolled and treated in Stage I reveals no permanent, serious adverse events due to treatment. The primary end measure is safety: number and severity of side effects and complications. The secondary end measures include variable neurological, neuropsychological and radiological evaluations (Positron Emission Tomography – PET) established in Core Assessment Program for Intracerebral Transplantations (CAPIT). Evaluations will be performed during on and off medication conditions at baseline, 6 months, 1 and 2 years after transplantation. The neurosurgical facility has state-of-the-art stereotactic equipment, CAT scan, MRI and Positron Emission Tomography.

Status: To be scheduled

- Filed for pre-IND guidance for trial with FDA
- Dr. Oleg Kopyov and Dr. Christopher Duma designing protocol