Applications for Celavie

At Celavie Biosciences LLC, we are developing regenerative stem cell therapies for the treatment of Parkinson's disease and other disorders of the central nervous system. The unmet medical needs for these conditions are significant, as they result in loss of basic function or mortality, and the need will only grow alongside the global population. Our therapies use undifferentiated allogeneic pluripotent stem cells to repair and restore damaged tissues, with early trials demonstrating safety and the promise of efficacy.

A key feature of Celavie's approach, which sets it apart from mainstream stem cell technology, is that the cells are not matured before use, as is the case with many adult stem cells. The theoretical premise of this approach is that undifferentiated stem cells are pluripotent and can read cues in the micro-environment into which they are injected, becoming any cell type required to repair tissues that have been damaged by chronic disease, use, or trauma.

A Novel Approach to Neurological Disease

We believe that Celavie's stem cells, with their restorative power and their versatility to become multiple tissues, represent humanity's best hope for curing many unaddressed or underserved degenerative diseases and injuries. We have shown in vitro that our stem cells are capable of maturing into a wide range of adult stem cells that can be applied to a number of diseases, such as:

- Parkinson's Disease (Dopamine Producing Neurons)
- Cerebellar Ataxia (Calbindin-Positive Neurons)
- Tendon and Ligament Injuries (Tenocytes)
- Bone Injuries (Osteoblasts)
- Joint Injuries (Chondrocytes)
- Myocardial Infarction (Cardiomyocytes)
- Diabetes (Pancreatic Cells)

Currently, Celavie's technology is undergoing clinical trials for its efficacy in treatment of patients with Parkinson's disease. Celavie recently conducted the first-in-human trial of stem cells in Parkinson's patients, with promising indications, and is now planning its Phase II clinical trials.

Phase I Clinical Trial for Parkinson's Disease in Mexico

- **Purpose:** To evaluate the safety of OK99 stem cells in treating patients suffering from Parkinson's disease
- **Conduct:** Hospital Angeles del Pedregal, Mexico City. Study approved by the Federal Commission for Protection against Sanitary Risks (COFEPRIS – Mexico's FDA equivalent)
- **Methodology:** Eight patients with moderate to severe PD not adequately controlled with medication were selected for the study. OK99 stem cells were injected into putamen. Patients were immunosuppressed with Cyclosporine for one month after injection. Patients were examined with Positron Emission Tomography (PET) using three radio markers (two per patient) to fully evaluate molecular changes in the brain after transplantation.
- **Time frame:** 2014-Ongoing

—more—

Addressing a Global Need

6.3%
Burden of disease stemming from central nervous system neurologic disorders & cerebrovascular disease[1]

$25 billion
Annual cost of Parkinson's disease in US[2]

$22,800
Per patient Parkinson's-related medical expenses ($12,800 higher than someone without PD)[3]

$6.3 billion
Indirect costs for a Parkinson's patient or family member helping with care[3]

$5 billion
Nursing home care-related costs for Parkinson's patients in US[3]

6,000 – 12,000
Number of young-onset patients (21-40 years old) diagnosed each year in US[4]

60,000
Number of new Parkinson's cases diagnosed each year in US[4]

1 in 50,000
Estimated number of US patients with Friedreich's ataxia[5]

1 in 100
Number of people carrying of the FA gene who do not exhibit symptoms[5]

[1] World Health Organization
[2] Parkinson's Association of the Rockies
[3] *Movement Disorders*, March 2013, International Parkinson and Movement Disorder Society
[4] American Parkinson's Disease Association
[5] Friedreich's Ataxia Research Alliance

- **Results:** Results are pending. To date, no tumors or lasting severe adverse effects have been reported.
- **Status:** Ongoing
  - Evaluations to be repeated 2 and 3 years after transplantation
  - Two-year follow up to be published in 2017
  - In the process of obtaining FDA pre-IND guidance for conducting larger controlled single-blinded randomized trial in US
  - Dr. Oleg Kopyov & Dr. Christopher Duma are designing protocol for larger controlled single-blinded randomized trial
- **Publication:** Trial registered at ClinicalTrials.gov website

Controlled Single-blinded Randomized Trial in US

- **Purpose:** To evaluate the safety of OK99 stem cells in treating patients suffering from Parkinson's disease
- **Conduct:** Hoag Memorial Hospital Presbyterian, Newport Beach, CA
- **Time frame:** 3 years
- **Methodology:** The trial is planned as a randomized, single-blinded study in which 20 patients with advanced to moderate PD will receive bilateral implantations of undifferentiated OK99 cells into the brain's putamen, with 20 patients serving as controls. All independent raters will be blinded to the condition of the patient. 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, 2 and 3 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 designing protocol.

Presently, Celavie is conducting pre-clinical trials of OK99 undifferentiated stem cells in animal models of diabetes mellitus type I, and further studies of cerebellar ataxia (effect of stem cell treatment on the animals' longevity) in collaboration with California State University, Northridge. Our research plan includes preclinical studies using OK99 stem cells for animal models of epilepsy, stroke and ALS. Our goal is to develop cells that are hypo-immunogenic and do not cause tumors. Unlike embryonic stem cells, OK99 cells have not produced tumors when implanted into immunodeficient rats. An equine open label study with 400 cases treated did not reveal any tumor formation during a three-year follow up.

The foundational theory of Celavie technology is that undifferentiated stem cells are able to react to the micro-environment into which they are injected and mature into multiple cell types dictated by their new surroundings. Unlike commonly used pre-differentiated cells, this would allow our undifferentiated cells to address diseases with complex multifactorial deficiencies in their entirety.

Through a purposeful, innovative union of science, medicine, technology and the marketplace, Celavie cultivates the natural healing powers intrinsic to the biology of cells to relieve suffering and deliver advances in medical treatment worldwide, elevating human potential today and for generations to come.

Our cells are not a last resort for the hopeless but a first line treatment for the hopeful. At Celavie Biosciences, we envision a future in which the scourge, suffering and wasted human potential caused by the global burden of disease has been eliminated through the power of science, leadership, collaboration and compassion.

Follow us at www.celavie.com and on LinkedIn and Twitter: @CelavieBioSci

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