Data Published in *Functional Neurology* Demonstrate that Global Kinetics' Personal KinetiGraph® (PKG®) is Uniquely Positioned to Enable Objective Assessment of Motor Fluctuations in Parkinson's Disease Patients

Unlike patient-reported motor diaries, PKG distinguishes among different groups of fluctuators and identifies high levels of dyskinesia among patients who deny having dyskinesia symptoms

PORTSMOUTH, NH USA, LONDON, UK and MELBOURNE, Australia, July 23, 2019 – Global Kinetics Corporation Ltd. today announced the publication of a study demonstrating that the use of data from its wearable FDA-cleared Personal KinetiGraph® (PKG®) provides an objective and more effective approach to assessing motor fluctuations in Parkinson's Disease (PD) patients compared with patient-reported motor diaries. Study results were published in *Functional Neurology*.[1]

"Motor fluctuations, including "wearing-off" and dyskinesia, are associated with increased disease severity and disability, and PD patients experience decreased quality of life as their response to medical therapy becomes less predictable," said Echo E. Tan, MD, Neurologist at Cedars-Sinai Medical Center and lead author on the publication. "Effectively managing motor fluctuations is complicated by the lack of objective assessment tools, leading patients and physicians to rely on direct observation in the clinic or patient reports, which may be unrevealing, incomplete and unreliable. The results of our study demonstrate that the fluctuation score calculated by the PKG system provides objective quantification of motor fluctuations. This may help improve routine management of PD patients and enable more objective assessments in clinical trials of PD therapies."

Parkinson's disease patients typically respond well to medical therapy in the first few years of their disease. However, approximately 40% of PD patients develop fluctuations of response to levodopa and dyskinesia after 4-6 years of treatment, which increases to 70% after long-term treatment of 9 or more years.[2-4] The PKG was developed to address the lack of objective measurement tools for movement disorders and quantifies the kinematics of PD symptoms, including tremor, bradykinesia and dyskinesia. A proprietary algorithm translates the raw data from these assessments into a fluctuation score (FS) that can distinguish between patients with motor fluctuations and those without.

In order to determine if the PKG could define motor fluctuation (MF) progression, study investigators correlated PKG fluctuator scores (FS) with clinical motor fluctuator profiles in a case-control cohort study of 60 PD patients attending the Movement Disorders Clinic at Cedars-Sinai Medical Center, Los Angeles, California. Of the 60 patients included in the study, six had incomplete data and were excluded from analysis. Key findings from the 54 subjects who completed a 6-day PKG trial and completed a standardized motor diary included and were included in the analysis are:

- Based on Wearing Off Questionnaire (WOQ9) and Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part IV scores patients were categorized based on the presence and extent of fluctuations, as follows:

  o Non-fluctuators (NF), N = 14
  o Early fluctuators (EF), N = 15
  o Moderate fluctuators (MF), N = 15

- o Troublesome fluctuators (TF), N = 10
- The groups varied significantly in terms of disease duration, which was progressively longer with increasing severity of clinical fluctuation and PD dopamine medication measured as levodopa equivalent dose (LED).
  - o LED was more than double in patients with troublesome fluctuations compared to those without fluctuations, while patients in the groups including early and moderate fluctuators reported equivalent daily dosages.
  - o MDS-UPDRS score increased significantly with the severity of fluctuations, with the highest scores recorded in those with troublesome fluctuations.
- Patients had a higher tendency to return the PKG than the motor diary (88% vs. 65%).
  - o 50% of the patients in the troublesome fluctuator group were excluded due to incorrect diary completion
  - o Compliance with the motor diary improved with decreasing severity of fluctuations
- PKG fluctuation score significantly differentiated EF and TF (p = 0.01), as well as dyskinetic and non-dyskinetic subjects (p < 0.005). In contrast, motor diaries could not distinguish the four study groups on the basis of average OFF time, while average time with dyskinesia distinguished NF and MF but did not distinguish among all four groups.
- PKG identified high levels of dyskinesia in patients who denied having dyskinesia.

The study authors conclude that the data support the use of the PKG fluctuation score as an objective tool for capturing and quantifying motor fluctuations as a mechanism for triaging PD patients. They also note that the PKG transcends language and cognitive barriers and time constraints in the clinic, which are challenges to obtaining accurate patient symptoms to effectively adjust PD treatment.

John Schellhorn, CEO of Global Kinetics Corporation, said, "The accurate recognition of motor fluctuations is essential for staging PD, determining treatment changes and identifying patients who are candidates for advanced therapies. To date, accurate assessment of motor fluctuations and other aspects of PD kinematics have been hindered by the lack of objective measurement tools. The results of this study add to the growing body of data supporting the clinical benefit of PKG as an objective tool for guiding treatment decisions that overcomes the limitations of physician observation and patient reporting. We believe that increasing adoption of the PKG will help to standardize and improve treatment for PD patients, and enable evidence-based approaches to optimizing care and outcomes for PD patients when they are first diagnosed and as their symptoms evolve over time."

References
[1] Tan EE, Hogg EJ, Tagliati M. The role of Personal KinetiGraphTM fluctuator score in quantifying the progression of motor fluctuations in Parkinson's disease. Functional Neurology. 2019;34(1):21-28.
[2] Schrag A, Quinn N. Dyskinesias and motor fluctuations in Parkinson's disease. A community-based study. Brain 2000;123:2297-2305.

[3] Ahlskog JE, Muenter MD. Frequency of levodopa-related dyskinesias and motor fluctuations as estimated from the cumulative literature. Mov Disord. 2001;16:448-458.

[4] Pahwa R, Lyons KE. Levodopa-related wearingoff in Parkinson's disease: identification and management. Curr Med Res Opin. 2009;25:841-849.