

Manus Neurodynamica US

Category:

Best Startup

Company Name:

Manus Neurodynamica US

Turnover and/or Funding:

A total investment of \$10 million was received. Funders include a total of 6 UK and US institutional investors, the European Commission, J&J and Innovate UK.

The Company has recently started to generate first revenues in the EU and is now progressing with a US-focused strategy, following US registration and establishing first US clinical reference centres, where the products are being implemented.

Sub-Category:

Medical Technology / Digital Health

Corporate history (creation, key milestones, main funding,...) Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):

The NeuroMotor Pen™ (NMP) platform is a unique digital biomarker platform for detection and quantification of movement and cognitive symptoms, using novel sensor technologies built into a digital pen with an analytical engine with AI Decision Support. The interface enables recording 'digital biomarkers' that provide objective and quantitative information about cognitive impairment and movement abnormalities. An AI algorithmic overlay supports differentiation between neurological disorders. NMP is the only device that measures both cognitive and movement symptoms.

Manus was founded to deliver NMP for non-invasive and low-cost digital neuro assessments anywhere needed in response to the need in an aging society. Neurological disorders are on the rise and the leading cause of disability [1]. Already 100 million American already suffer from one/more neurological disorder [2] and Parkinson's (PD) is the fastest growing problem [3].

By 2037, there will be an increase from currently 1 million to 1.6 million patients with PD with a cost burden of 79 billion [4]. However, the bigger problem is that there are

more than 10 million people with tremors, who worry that they may develop PD. Given that primary care does not diagnose or treat neurological disorders and is often insufficiently equipped to provide reassurance to those with benign symptoms, specialist clinics are often overburdened, making it difficult to make a timely diagnosis and provide personalized treatments with regular follow up. A more patient centred approach is needed [5].

In addition, even for specialists, making differential diagnostic decisions is difficult. A clinical diagnosis is mainly based on clinical symptoms. The only tools are clinical rating scales (observation) and brain scans, but these are expensive, uncomfortable for patients and not conclusive.

Tremor is the major symptom for 90% of Parkinson's sufferers [6, 7, 8] and an extremely complex feature. Differentiating between a Parkinsonian tremor and other tremor disorders is challenging even for specialists [9]. The separation of PD from Essential Tremor (ET) accounts for about half of the misdiagnoses [10]. The lack of tremor measurement equipment in the clinic is part of the cause for not being able to differentiate between PD and ET. Subtle tremors are often already present in prodromal stage before a diagnosis can be made [11]. A major breakthrough in establishing an early diagnosis lies in measuring the earliest changes in the neuromuscular system, and in particular tremor, due to Parkinsonism [12, 13, 14, 15].

Manus' proposition is streamlining pathways with NMP, enabling primary care and 'provider status' pharmacies to implement prevention screening and reassure those with benign problems while triaging those who need to be seen by specialists. In movement disorder settings, NMP is used as 'aid to differential diagnosis'. The diagnostic accuracy improved from 38-65% (reference neuropathologic findings) [16, 17] to 80% at the first specialist appointment [18]. This reduces the need for multiple appointments over a 6-24 month period – reducing appointments and costs.

FDA awarded "Breakthrough Device" status for differential diagnostic decision making in Tremor. In April 2024, the first NMP product was FDA authorized for symptom assessment.

History of the development of the solution/product (Intellectual Property, preclinical and clinical data, development collaborations):

The NMP product and clinical claims are based on sound scientific work towards the solution and grounded in deep understanding of the current challenges within the standard of care. At the inception, the founder instigated the DiPAR project (diagnosing Parkinson's) and the European Commission awarded €1.8 million of grant funding (under grant agreement 262291) to collaborate with world class R&D performers in the

DiPAR project to progress R&D towards product development with clinical validation studies. The consortium included four academic collaborators, including the University Medical Centre Groningen (Netherlands) and four SMEs. Clinical KOLs involved were Profs Leenders and van Laar (UMCG) and Prof Mark van Gils (signal processing and AI for digital health solutions at the technical research center of Finland).

The DiPAR project was successfully completed after 4 years and resulted in a clinically validated pre-production prototype with claims for differential diagnostic and monitoring use that were published in peer reviewed journals, reporting on:

- NMP standardised drawing tasks for assessment [19,20,21,22,23];
- Accurate quantification of symptoms and rating medication effects, similar to the Purdue pegboard task (reference measure) [19, 21].
- NMP scores match standard Unified Parkinson's Disease Rating Scale [19,21].
- High reproducibility [20].
- Accuracy > 80% differential diagnosis of Parkinson's vs other; sensitivity 86% [22,23].
- Usability: Automated record keeping; Can be used at home by non-experts [21,23]

Following DiPAR, Manus progressed productization and the following milestones were achieved:

- Successful product development, following prototype development. During this time Manus forged a collaboration with Schwann-Stabilo for co-development of the NMP stylus. An exclusive manufacturing and supply agreement with quality agreement is in place with Stabilo.
- Further successful EU clinical trials (publication in progress)
- A study of 150 patients in the Northumbria NHS Trust' (Prof R Walker), evaluated User acceptance of the NMP system and its graphical task regimen in clinical setting: 97% reported they enjoyed the drawing tasks.
- EU CE mark
- Quality procedure for medical device manufacturing, following ISO 13485 QMS standard
- FDA 'Breakthrough Device Designation'
- FDA pre-sub meeting re US regulatory strategy & De novo approach
- FDA data development plan and pivotal study agreed with FDA
- FDA authorized product: class 2 approval for symptom assessment.
- Design History File, Device Master Record, Device History Record, provides 'jump-start'/foundation for future 510(k) & De Novo submissions.
- FDA QSR requirements
- Signed up US academic hospitals with Key Opinion Leaders for clinical trial: Prof Irene Litvan (UCSD), Prof Travis Turner (MUSC), Prof Joohi Jiminez-Shahed (Mount Sinai, NYC), Gammon Earhart (Washington University).
- Signed agreement with J&J for use of NMP in CAR T-cell therapy to detect early signs of neurotoxicity (adverse effect).

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:

The NMP innovative concept enables healthcare professionals (HCPs) to non-invasively test for impairment of the brain's extrapyramidal system that controls accurate movements. Novel sensors along with analytics were developed with specific graphical assessment tasks for biomarker extraction to reveal what cannot be seen/interpreted with the naked eye. The analysis of fine motor skill with NMP reveals specifics of the nervous system's motor control strategies and which of these are impaired, which can be linked to the underlying movement or cognitive issue.

Additionally, novel NMP AI methods were developed to provide additional decision support. The innovation was validated within the care setting and correlated with current clinical standards.

For the first time, this enables a faster diagnosis with increased differential diagnostic accuracy compared with the current standards of care. FDA awarded breakthrough designation, making NMP the first aid to diagnosis in Parkinson's.

In addition, NMP implements automated digital versions of clinical pen and paper based cognitive assessment tasks. Assistants may complete the test, freeing up specialist time and reducing expenditure. Digital storage of assessments enable longitudinal monitoring.

Patients with neurological disorders often exhibit a combination of movement and cognitive symptoms, but these are difficult to distinguish. NMP assesses both at the same time to confirm whether the impairment has an underlying cognitive or movement problem.

The NMP implementation has enormous impact potential both in the developed world as well as in the developing world. NMP can aid the specialist diagnosis: Distinguishing benign tremors from Parkinson's is problematic and mostly based on subjective examination with reported accuracy levels in early symptomatic stages when seen by the specialist for the first time of 38%-65% [24, 25]. For 75% of the patients, it takes 6 - 24 months to confirm a clinical diagnosis Parkinson's. Brain scans are stressful and intrusive, using radioactive tracers. NMP in EU trials in specialist centres increased accuracy at first appointment for from 50% to 80% [26]. Health economic benefits include a reduced number of appointments & faster diagnosis, reduced number of brain scans and patients stay well for longer. For the patient it means a step increase in quality of life once on treatment and benefiting from lifestyle adjustments.

NMP is the first device that is sufficiently sensitive for the early detection of Immune effector cell-associated neurotoxicity syndrome (ICANS) – neurotoxic events – which frequently occurs as adverse effect of CAR T-Cell cancer treatment. It is widely known there is a need for an objective, reproducible, easy-to-use, and practicable tool that can be used by all health care providers and possibly caregivers to recognize and assess ICANS in the inpatient or outpatient setting [29]. The earliest manifestations of ICANS include tremor, dysgraphia, general deterioration of fine motor skill and impaired attention [27,28,29]. NMP can detect this with high sensitivity. Telehealth monitoring patients with NMP, following CAR T-cell treatment, reduces ICANS risk, which could otherwise in some cases lead to death. Patients no longer need to stay in the hospital for observation. An award from innovation giant J&J was received and an agreement signed for trialling and implementation.

Please provide appropriate references (PubMed, Abstract, Website):

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