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Setting the TEMPO: A Phase 3 Program to Investigate Tavapadon, a Selective D1/D5 Partial Agonist, for Parkinson's Disease

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CONCLUSIONS

- The TEMPO program will establish the efficacy, safety, and tolerability profiles of tavapadon, a selective D1/D5 partial agonist, as a promising next-generation treatment for PD
- As there have been no US Food and Drug Administration–approved treatments indicated as both monotherapy and levodopa-adjunct therapy for PD in over a decade, the results from the TEMPO program may support use of a new treatment option for PD

INTRODUCTION

- Tavapadon is a first-in-class, partial agonist that is highly selective at dopamine D1 and D5 receptors[1,2]
- By selectively targeting D1/D5 receptors, tavapadon may improve motor symptoms while minimizing adverse events generally associated with traditional D2/D3 receptor agonists
- Previous phase 1b/2 studies support phase 3 investigation of tavapadon[1,2]

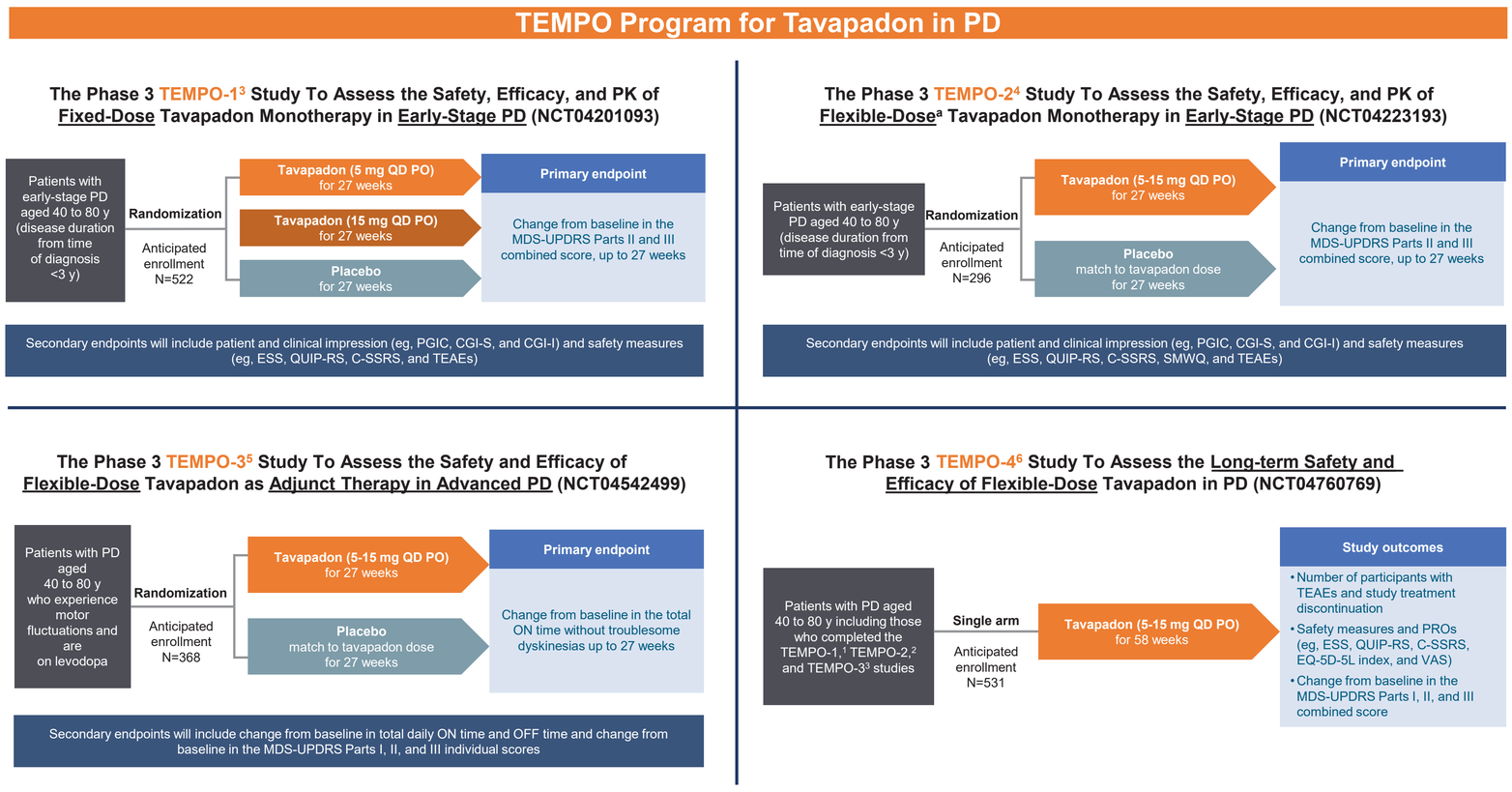
OBJECTIVE

- To describe the design of the phase 3 TEMPO program that will evaluate the efficacy, safety, and tolerability of once-daily (QD) tavapadon in early-stage and advanced Parkinson's disease (PD)

TEMPO STUDY DESIGNS

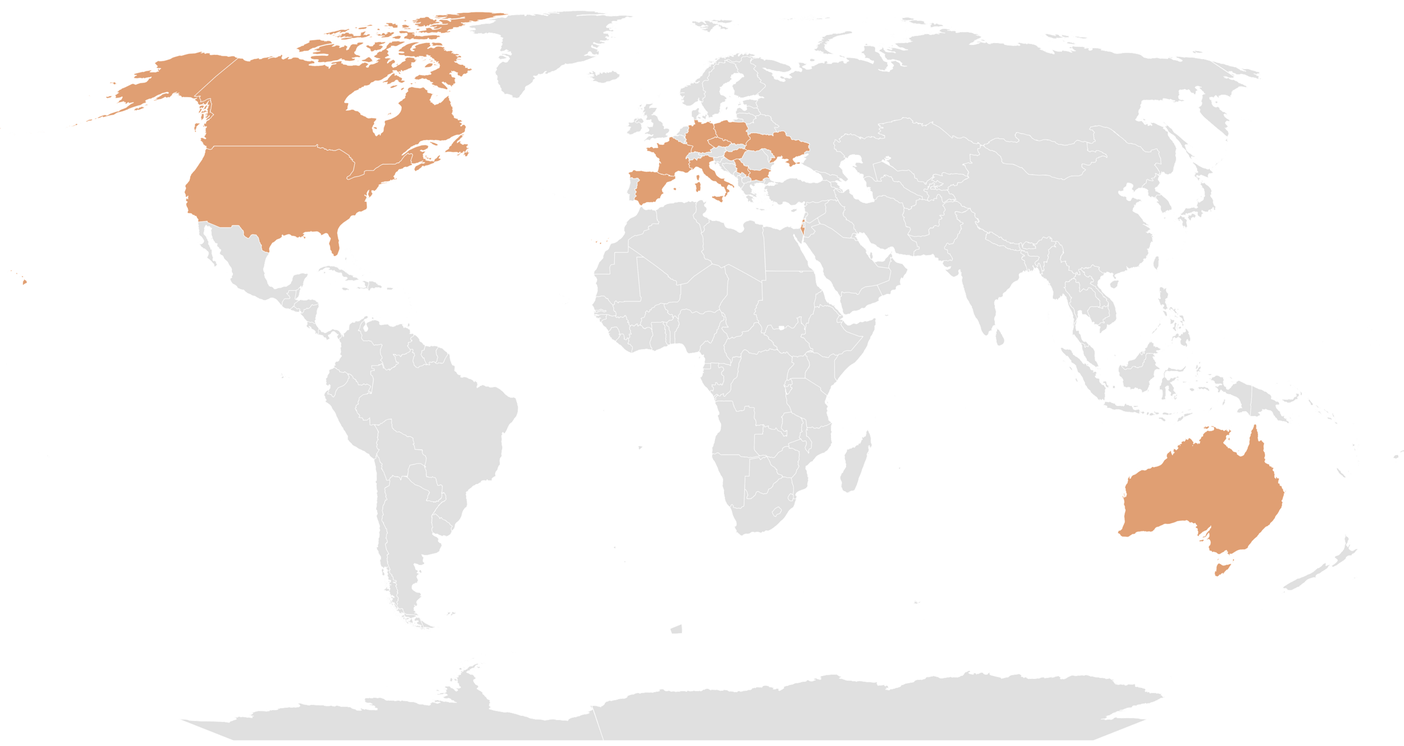
- The eligibility criteria and study designs, including the primary endpoints of the TEMPO studies, are shown in Figure 1
  - TEMPO-1 (NCT04201093) and TEMPO-2 (NCT04223193) are phase 3, randomized, placebo-controlled, 27-week studies of tavapadon monotherapy as fixed doses (5 and 15 mg QD) and flexible doses (5-15 mg QD), respectively, in patients with early-stage PD (Movement Disorder Society–Unified Parkinson's Disease Rating Scale [MDS-UPDRS] Part II score ≥2 and Part III score ≥10; modified Hoehn and Yahr stage 1, 1.5, or 2)[3,4]
  - TEMPO-3 (NCT04542499) is a randomized, placebo-controlled, 27-week study of tavapadon (flexible dose: 5-15 mg QD) adjunctive to levodopa in patients experiencing motor fluctuations (modified Hoehn and Yahr stage 2, 2.5, or 3 in the "ON" state, minimum 2.5 h of "OFF" time on 2 consecutive days)[5]
  - Rollover participants who complete TEMPO-1/-2/-3 may be eligible for the open-label, 58-week TEMPO-4 study (NCT04760769); de novo patients with PD are eligible to participate at US study sites (aged 40-80 years; diagnosis of PD consistent with the UK PD Society Brain Bank diagnostic criteria; modified Hoehn and Yahr stage 1, 1.5, 2, 2.5, or 3)[6]
- TEMPO studies will monitor for excessive daytime sleepiness (via Epworth Sleepiness Scale) and impulsive compulsive disorder (via Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease–Rating Scale)
  - These side effects are associated with currently approved D2/D3 selective dopamine agonists[7,8]
- COVID-19 mitigation strategies employed for TEMPO studies have included the use of home health visits, telemedicine, and direct-to-patient delivery of study drug
- 14 countries have participating sites for one or more TEMPO clinical studies (Figure 2)
  - Study sites with patient enrollment in the TEMPO program are located in Australia, Bulgaria, Canada, Czech Republic, France, Germany, Hungary, Israel, Italy, Poland, Serbia, Spain, Ukraine, and the United States

Figure 1. TEMPO program for tavapadon in PD.



CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impression–Severity of Illness; C-SSRS, Columbia-Suicide Severity Rating Scale; ESS, Epworth Sleepiness Scale; EQ-5D-5L, EuroQol 5-Dimension 5-Level; MDS-UPDRS, Movement Disorder Society–Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease; PGIC, Patient Global Impression of Change; PK, pharmacokinetics; PO, oral; PRO, patient-reported outcome; QD, once daily; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease–Rating Scale; SMWQ, Study Medication Withdrawal Questionnaire; TEAE, treatment-emergent adverse event; VAS, visual analog scale. [a]Patients received dose titrated up to 15 mg QD PO, based on individual patient tolerability.

Figure 2. Countries with participating clinical sites in the TEMPO program.



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