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Prana Back In The Clinic With PBT434 For Parkinson's Disease

Prana says it has commenced screening and recruitment for its up-to 88-patient, phase I trial of PBT434 for Parkinson's disease, with first dosing expected "soon".

Prana executive chairman Geoffrey Kempler and recently appointed chief medical officer Dr David Stamler said they were giving a series of briefings to investors and media on the progress of the trial and the company.

Mr Kempler said that the company had funds for about 12 months which would take it beyond the end of the two-part trial.

In 2014, Prana fell 70 percent on news that its imaging trial of PBT2 for Alzheimer's disease did not meet its primary endpoint of reducing amyloid beta plaques having earlier climbed when a phase II trial of PBT2 for Huntington's disease met the primary endpoint of safety and tolerability but met only one secondary endpoint for cognitive efficacy of several secondary endpoints (BD: Feb 18, 19, Apr 1, 2014).

In 2015, Prana said the US Food and Drug Administration had issued a partial clinical hold limiting the dose of PBT2 for patients with Huntington disease and last year, Prana said that European regulators wanted more pre-clinical work before allowing a phase III trial of PBT2 for Huntington's disease (BD: Feb 13, 2015; Dec 23, 2017).

Today, Mr Kempler and Dr Stamler said that PBT434 was a completely separate molecule to PBT2 and targeted iron inside cells rather than PBTs mode of action which targeted copper and zinc outside cells.

Dr Stamler said that PBT434 was shown to bind to iron and remove it from the cells for excretion and that iron in cells had been implicated in Parkinson's disease.

In March, Prana published mouse data showing evidence for PBT434 to prevent the loss of neurons and improved function for multiple system atrophy (BD: Mar 7, 2018).

The company described the compound as “the first of a new generation of small molecules from the quinazolinone class of drugs that was specifically designed to block the accumulation and aggregation of alpha-synuclein, an abundant brain protein widely believed to be involved in the pathogenesis of Parkinson’s disease and related disorders”.

Prana said at that time that alpha-synuclein was of “great interest” because aggregated forms of the protein were considered a pathological hallmark of Parkinsonian conditions and were a recognised therapeutic.

Today, Dr Stamler said that the company had undertaken further pre-clinical work in dogs to determine a therapeutic dose window prior to the first human clinical trial.

Dr Stamler said that the first part of the trial would be a single ascending dose study of up to 48 healthy volunteers, in cohorts of eight subjects per dose, to investigate the pharmaco-kinetics, safety and blood levels of the drug, as well as finding the maximum tolerated dose.

Dr Stamler said that second part of the trial would use a multiple ascending dose model with daily dosing of three different levels of PBT434 for one week.

Mr Kempler said that when Dr Stamler was appointed chief medical officer and head of clinical development, he brought with him his San Francisco-based team from Auspex Pharmaceuticals which was responsible for the approval of Austedo, or deutetrabenazine, for the treatment of chorea associated with Huntington’s disease in 2017 and was acquired by Teva Pharmaceuticals for $US3.5 billion (BD: Jun 5, 2017).

Mr Kempler said that PBT2 effectively had been shelved but the company was considering possible partner or licencing alternatives.

“We have thousands of molecules,” Mr Kempler said.

“And an active drug discovery program, Dr Stamler said.

Prana was unchanged at 4.2 cents.